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BUREAU OF HYGIENE AND TROPICAL DISEASES.

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THE DIAGNOSIS OF KALA AZAR.

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Kala azar, or visceral leishmaniasis, once looked upon as a disease of the tropics, is now known to occur in all the continents except Australia, and in a variety of climates, ranging from the frankly tropical to the temperate.

Increasing facilities for world travel and residence in countries where the disease is endemic, will, almost certainly, result in its occurrence in individuals returning to their own countries from such areas. This introduction of cases into countries where the disease does not normally occur, and cannot spread, has already been exemplified on an exaggerated scale as a result of the war. Thus, in Great Britain alone, some hundreds of cases have already been diagnosed in persons returning from war areas, and this number certainly does not represent the total number of cases introduced during the same period. What has happened in Great Britain must also have occurred in other countries to which persons from war areas have returned. The importance of making an early diagnosis in these cases, therefore, needs no further justification, and this is the more important in those countries where the transmitting vector exists, since such cases might lead to the spread of the disease.

The account of methods of diagnosis given below is not meant to be exhaustive and only those procedures are described which have proved reliable in practice and which can be applied in any laboratory without the use of special equipment or materials.

The most practical approach would, perhaps, be to consider a hypothetical case presented by the clinician for diagnosis and to describe the sequence of steps to be taken in establishing a diagnosis of kala azar. Such a case is likely to be one with a history of a long-continued fever the cause of which previous investigation along orthodox lines has failed to elucidate. In any investigation aiming at the making of a definite diagnosis of kala azar it must always be borne in mind that the only infallible criterion is the demonstration of *Leishmania donovani*, either in the form of Leishman-Donovan bodies or in the form of flagellates in culture.

If one presumes, then, that the possibility of the case being one of kala azar has been envisaged, the following investigations should be carried out.

History.

This is important owing to the sometimes prolonged incubation period. If the patient has lived, even for a short time only, in any area where kala azar is endemic, the case for this disease is strengthened.

Such areas would be :—

In Asia.—India, China, Central Asia, Transcaucasia, Turkestan.

In Europe.—Any country bordering on the Mediterranean sea, or immediately neighbouring countries such as Bulgaria.

In Africa.—The Sudan and Kenya at least as far south as Nairobi, Abyssinia, parts of the French possessions and the countries bordering on the Southern shores of the Mediterranean.

In America.—Various countries of South America such as Brazil and Argentina.

In most of these areas, except the Mediterranean, kala azar is found to attack people of all ages, especially older children and young adults. In the Mediterranean area the great majority of cases occurs in young children, probably over 60 per cent. being in children up to two years old. This age incidence, however, appears to be less well-marked in the case of non-indigenous persons exposed to infection and numerous cases of the disease have been recorded in such adults.

Clinical examination.

The patient has been ill for some time and therefore should present the usual signs and symptoms of kala azar.

There is generally a history of *long-continued fever*, remittent or intermittent, usually commencing gradually, but sometimes suddenly. There is often a double or even triple rise of fever during 24-hour periods, seen when 4-hourly charts are kept. The fever is differentiated from that of *typhoid fever* by a relatively rapid pulse and the almost complete absence of the marked toxaemia noted in that disease. From the fever of *malaria* it is distinguished by the relative absence of pains in the back and limbs, and of headache. The *spleen and liver, especially the former, are enlarged*, and there may be enlarged lymphatic glands in various parts of the body. The initial fever is often followed by a period of apyrexia, during which the enlargement of the spleen progresses. Appetite is usually not much impaired but there is an *increasing degree of anaemia and emaciation*. The hair becomes dull and dry, and may fall out. Accompanying the anaemia there is a *marked leucopenia*. In the later stages *emaciation* is extreme and the *abdomen protrudes markedly*, owing to the splenic enlargement, often accompanied by ascites.

Laboratory Investigations.

1. *The aldehyde or formol gel test.*—To 1 cc. of patient's serum in a Durham's or similar tube, 1 drop of formalin (40 per cent. formaldehyde) is added and the two liquids are mixed by shaking. A positive result is indicated by gelification of the mixture, accompanied by a whitish opacity. Gelification, unaccompanied by opacity, does not constitute a positive result. The change in the mixture is usually evident in a few minutes and should, in any case, be complete within half an hour.

This test is reliable in developed cases of kala azar but may give a negative result in the first four months of the infection.

2. *Microscopical examination of the peripheral blood.*—For this the blood slide must be prepared in a special way. A drop of finger blood is placed near the end of a glass slide. The end of a second slide is drawn backwards along the first slide until it meets the drop of blood, which now spreads out along the straight end of the second slide. This is now pushed along the first slide, making an angle of about 45°, until it is seen that the blood is nearly exhausted. At this point the pushing movement is stopped and the spreader slide is raised abruptly. The resulting blood smear has a straight-edged and rather thick termination ; in this straight edge there will be found a great

concentration of leucocytes. The slide is fixed and stained, in the usual way, with Leishman or Giemsa stain. The thick edge is then examined for the presence of Leishman-Donovan bodies inside the leucocytes. These bodies are to be found in the large monocytes and, less commonly, in the polymorphonuclears. In skilled hands this technique gives a positive result in 70–80 per cent. of proved cases of Indian kala azar, but the percentage is said to be less in other types of the disease.

3. *Culture of the peripheral blood.*—About 2–5 cc. of blood, obtained by venepuncture, are added to four times the volume of citrated saline solution (sodium chloride 0·85 per cent., sodium citrate 1·5 per cent.) and the mixture is centrifuged. Alternatively, the mixture may be kept at room temperature or in an incubator at 22°C. for some hours to allow the cells to settle. The deposit consists of red cells and leucocytes, and some of the latter will contain Leishman-Donovan bodies if these are present in the specimen. With a capillary pipette a part of the deposit, especially the more superficial layer containing most of the leucocytes, is aspirated and sown in three or four tubes of NNN medium. These tubes are incubated at 22°–24°C. Flagellated *Leishmania* may be found in them after about 7 days, but they should be kept under observation for three weeks. Eleven or twelve days is the average time for the first detection of flagellates.

In untreated cases of Indian kala azar this technique should give a positive result in well over 90 per cent. of cases. Any examination of the peripheral blood, whether direct microscopic or cultural, is likely to give negative results once specific treatment has commenced, since one of the earliest effects of this is to cause disappearance of parasites from the peripheral circulation. For this reason examination of the blood should be confined to untreated cases.

The method of preparing NNN medium is given below :—

i. Dissolve by boiling 14 gm. of agar.
6 gm. of sodium chloride.
900 cc. of distilled water.

ii. Place this, in 4 cc. amounts, in test tubes of 6 in. × ¾ in. Plug with cottonwool and sterilize in an autoclave for 20 minutes at 1½ atmospheres.

iii. Cool the tubes to 50°C. in a waterbath and then add, with aseptic precautions, 15 drops (1 cc.) of whole rabbit's blood to each tube. Roll the tubes to mix the blood and agar.

iv. Allow to set in an almost horizontal position and, when quite solid, cap with deep rubber caps.

v. Incubate overnight at 37°C. to test for sterility and at the same time to express the water of condensation.

vi. Inseminate into the water of condensation.

vii. Incubate at 22°–24°C.

4. *Liver puncture.*—For this purpose a 5 or 10 cc. all-glass syringe is best, but any type of this size can be used. The needle is of the length supplied with such syringes, *e.g.*, 21 or 22 s.w.g. and 35 mm. long. It is all-important that the syringe and needle, when used, should be *absolutely dry* as, otherwise, the Leishman-Donovan bodies may be distorted and difficult to recognize. The patient lies on his back with his thorax and upper abdomen exposed. A point for the puncture is selected in the mid-axillary line between the two lowest ribs in this line, and a dab of tincture of iodine applied to this point. The needle of the syringe is placed on the skin in the centre of the coloured area and, with a quick jab, is thrust through the skin only. The patient usually makes some slight movement but can be assured that this slight prick is the worst he has to face. The needle is then quickly thrust fully in, between

the ribs, in a direction towards the opposite side of the body and somewhat upwards. As this is done, both hands should be in use, the left supporting the syringe near the needle and the right ready to withdraw the plunger. This should be done *immediately* the needle is thrust in, and the latter should be withdrawn at once along the line of entry. *Do not wait to see the entry of any fluid contents into the syringe*—this is neither necessary nor desirable—in fact, if the barrel of the syringe contains even a small amount of material the puncture is not a good one. There should be no more material than is contained in the small glass nozzle of the all-glass syringe. The contents of the needle are now ejected on to a glass slide and smeared out with another slide as in making an ordinary blood smear. When this is done, about 1 cc. of sterile citrated saline solution is sucked up into the syringe, and the fluid is then sown in 3–4 tubes of NNN medium. The slide is fixed and stained with Leishman's or Geimsa's stain, and will usually give the diagnosis at once by disclosing the presence of Leishman-Donovan bodies. The cultures are to be incubated at 22°–24°C. and should yield a culture of flagellates within 7 days, but should be kept under observation for not less than a fortnight. In following this technique the needle probably traverses the lower margin of the pleura, but this appears to have no ill-effects.

5. *Spleen puncture.*—This procedure has been placed after liver puncture only because of the almost universal opinion of the great danger inherent in the operation of spleen puncture. This fear is not easily understandable by those accustomed to use the technique for the diagnosis of kala azar because, if it is properly performed, the risk of accident would appear to be very small. The author has performed thousands of spleen and liver punctures without, so far as he is aware, any untoward results. The routine procedure is to give 30 grains of calcium lactate the night before, and 30 grains again just before the operation, but it is at least doubtful if this has any appreciable effect in increasing the coagulability of the blood. If considered necessary, coagulability may be tested and the puncture postponed if it is much below normal.

Spleen puncture may be performed on any patient whose spleen projects below the costal margin. In this case an assistant is necessary. A dab of iodine is placed on the abdomen over the most convenient part of the projecting spleen. *The latter is now supported by an assistant* who places one hand on the abdomen of the patient and supports the organ from below its level in the abdomen. The remaining procedures and precautions are exactly the same as those described under liver puncture, the needle, in this case, being thrust upwards and backwards into the spleen and withdrawn *immediately* along the same line *without any effort to see if material has entered the syringe.* The parasites are likely to be more numerous than in the material obtained from the liver, and this is probably the procedure of choice in skilled hands. In untreated cases, microscopical examination of the material obtained, combined with the results of culture, should give a positive result in every case.

6. *Sternal puncture.*—Although this has a special place in the study of blood disorders and can be employed in the diagnosis of kala azar, it is more unpleasant to the patient than either spleen or liver puncture, and is also less efficient for the demonstration of Leishman-Donovan bodies. Leishmania will usually be found quite easily in the marrow of untreated patients, but there are, undoubtedly, cases in which the parasites are present only in very small numbers in the marrow, though they are numerous in the liver and spleen of the same patients. Examination of the bone marrow has one advantage over other methods, but this is of little benefit to the patient as it applies only to examinations *post mortem.* After death, Leishman-Donovan bodies tend to disappear with the decomposition of the body, but are often recognizable in the bone marrow after they have disappeared from tissues like the spleen and

liver, which are, perhaps, accessible to bacterial contamination at an earlier stage than the bone marrow. The technique of sternal puncture is simple and the details are given below. Any 10 or 20 cc. syringe with good suction and a short, stout needle is suitable, but it is preferable to use one of the special syringes made for the purpose. These have a stilette and a stop, capable of adjustment, to prevent the needle penetrating too far.

The patient lies on his back with a support under the shoulders and the head thrown back. Any part of the sternum may be punctured, but the lower part of the *manubrium* is probably the site of election. This area is anaesthetized by a local anaesthetic, care being taken to infiltrate the periosteum.

The *thoroughly dry* needle, with stilette, is pushed into the joint between the manubrium and body of the sternum. The butt of the needle is then lowered until nearly parallel with the long axis of the sternum and the point is pushed in an upward direction until it is felt that the outer table of the bone is pierced. A boring movement of the needle may assist penetration. The stilette is now removed and the needle is pushed through the marrow, which is forced into the lumen. This is usually all that is necessary before withdrawing the needle but, if more tissue is required, the *thoroughly dry* syringe may now be attached and suction applied. This always causes pain or, at least, a very unpleasant sensation. The needle is immediately withdrawn and the wound sealed with friar's balsam.

The contents of the needle are now squirted out on to a slide, and further slides are prepared from the material obtained. From the material remaining in the syringe culture tubes are inoculated as described in the case of liver puncture. The slides are stained in Leishman or Giemsa stain, and examined for Leishman-Donovan bodies.

7. *Gland puncture.*—This method has been recommended as a reliable procedure for the diagnosis of kala azar in the Anglo-Egyptian Sudan, and has also been used in the Mediterranean area. The glands punctured, in the Sudan technique, are the lower group of the superficial inguinal lymph glands disposed along the long saphenous vein. The skin is sterilized, a gland is lifted up and steadied above the thumb and forefinger of the left hand, and a *dry* sterile No. 16 hypodermic needle thrust into it and allowed to remain *in situ* for a few seconds. A syringe body may be attached to the needle to apply suction, but this is not necessary. The needle is then withdrawn and the contents blown out on to a slide by attaching a syringe body if this has not already been done. The material is smeared out, stained with Leishman or Giemsa stain, and examined for the presence of Leishman-Donovan bodies. As before, culture tubes should also be inoculated.

8. *Complement fixation test.*—Various tests employing the principle of complement fixation have been used by different workers, but none could be considered completely satisfactory until the introduction of the reaction utilizing an antigen prepared from the human tubercle bacillus according to the method of Witebsky, Klingenstein and Kuhn (1931). The test, originally devised for the diagnosis of tuberculosis, gave indifferent results in this disease but, curiously enough, has proved of the greatest value in the diagnosis of kala azar.

For the method of preparation and use of the antigen the original papers, to which references are given, should be consulted, but the procedure, in general terms, is as follows. The haemolytic system of method No. 4 of the Wassermann reaction, as laid down by the British Medical Research Committee, is used together with a maximum quantity of the antigen which does not interfere with 1 m.h.d. of complement, and a 1 in 25 to 1 in 100 dilution of serum. To give an idea of the high value of this test a few figures may be quoted. In a series of 434 cases sent for diagnosis Sen Gupta (1943) obtained

positive reactions in 97 per cent. otherwise proved to be cases of kala azar, while a large number of controls of all kinds gave negative results.

This test has, more recently, been modified by the use of other acid-fast organisms such as *Mycobacterium phlei* and the so-called leprosy bacillus of Kedrowsky, Lleras, Bayon, and Duval instead of the human tubercle bacillus for the preparation of the antigen. These organisms are easily cultivated and therefore readily available when required. In tests carried out with an antigen prepared from these organisms the following results were obtained. Out of 260 proved cases of kala azar, 241 gave positive reactions, 16 doubtful reactions, and three negative reactions—percentage of positives 93. Out of 604 controls, 99 per cent. gave negative reactions.

Evidence of cure after treatment.—This should be considered together with diagnosis because insufficient treatment may lead to relapse, and in such cases a final cure is more difficult to attain and may even not be achieved.

In most cases, when splenic enlargement has disappeared and in other respects the patient appears well, the question arises " should treatment now be stopped ? "

Here, again, the only safe criterion is the demonstration that no parasites remain in the body. This can never be a procedure of the same certainty as demonstration of their presence because in a patient who is nearly cured they may be extremely few in number. The most reliable procedure in demonstrating cure is to perform a liver puncture and inoculate as large a number of tubes of NNN medium as possible. These should be examined for three weeks. If all are negative after this period the presumption of complete cure is strong.

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SUMMARY OF RECENT ABSTRACTS.*

II. YELLOW FEVER.

Epidemiology.

The Yellow Fever Research Institute at Lagos completed a successful year with a full staff for the first time since before the war (p. 838). Investigations were initiated into the distribution of yellow fever in Nigeria, and protection tests over a wide area showed 16 per cent. positive results. The results of tests revealed that there had been an outbreak within sight of Lagos, although the town itself appears to have escaped, possibly because of the relatively low density of *Aëdes aegypti* or a poor carrying power in the local strain. Three monkeys shot in the vicinity gave strongly positive tests.

Important experimental work on the susceptibility of mice of different ages to subcutaneous injection of yellow fever virus resulted in the useful practical observation that, for the mouse-protection test, animals less than 8 days old should be used, and small amounts of virus. This makes it possible to detect a higher proportion of healthy positive sera.

*The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1946, v. 43. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

The significance of varying susceptibility of animals to yellow fever virus and of varying vector efficiency of varieties of *Aëdes aegypti* is brought out by experiments in mice and " bush-babies " and in mosquitoes ; and the important bearing of inherited characters on susceptibility and invasiveness may be far-reaching.

The Expert Commission on Quarantine of UNRRA in its Third Report (p. 124) has advised the inclusion in the endemic zones of yellow fever certain areas additional to those originally delineated and adopted in December 1944. In Africa, the additional area is the Barotse Province of Northern Rhodesia ; and in the Western Hemisphere, alteration of the previously defined areas has been recommended as a result of the occurrence of cases of yellow fever in Venezuela and in the States of Minas Gerais and Goyaz in Brazil. Two maps, reproduced from *Epidemiological Information Bulletin*, illustrate the African and South American areas respectively (pp. 125, 126).

Yellow fever areas are discussed at length by DE PAULA SOUZA (p. 126) with special reference to South America. The Pan-American Sanitary Bureau suggested to the Expert Commission that three classes of areas should be distinguished : (1) Endemic areas where cases have occurred and where conditions favour its recurrence ; (2) areas where the risk of becoming infected exists ; (3) potentially infectible areas where an *Aëdes aegypti* index of 0·4 or higher exists. The National Department of Health of Brazil pointed out that modifications were necessary as infected areas in that country varied in character. An *aegypti* index of 0·4 and less is attainable in S. America, but in Africa a goal of 1 per cent. is regarded as a good first step.

No urban outbreak attributable to *A. aegypti* has occurred in America since 1933, though transmission by *Aëdes aegypti* has often followed jungle yellow fever in Brazil, Bolivia and Colombia between 1934 and 1938 and once in the Acre territory of Brazil in 1942. Anti-mosquito campaigns are yielding good results ; 42,946 of 44,859 localities were completely freed in 1944, and *A. aegypti* has been eradicated from eight States. Shifting of areas still occurs in Colombia and Brazil. In 1945, an outbreak in the States of Goyaz and Minas Gerais, after three years' quiescence, caused 101 deaths in a few months. In July 1945, 18 deaths occurred in Venezuela and 14 in Colombia, and in May there were 6 deaths in Peru and 2 in Bolivia.

ANTUNES and CASTRO (p. 643) describe the endemic yellow fever area in Brazil and point out that the demarcation plan of UNRRA does not distinguish between endemic and epidemic areas.

The Fourth Report of the Expert Commission (p. 1135) modifies somewhat the endemic areas in Brazil, and also excludes from the endemic area in Africa an area 10 kilometres round the town of Asmara in Eritrea, subject to satisfactory monthly *Aëdes* indices. At its meeting the Commission also discussed the question of differentiating administratively between endemic and epidemic yellow fever areas, and gave an account of experiments to test the efficacy of anti-yellow fever vaccine made at the Pasteur Institute at Dakar (see below).

DIAZ (p. 213) describes an outbreak of jungle yellow fever in Venezuela in 1944, which occurred in an area close to the Andean range in the States of Barinas, Bolívar and Táchira, near the Colombian border. Formerly, Bolívar had been considered the only endemic yellow fever zone in Venezuela. It is supposed that in the whole area affected, there must have been about 120 cases, with a death rate of 70 per cent. Immediate precautionary measures were taken, and by the end of the year 28,263 vaccinations had been made.

LAIRET (p. 437) refers to the Cuyuní Valley outbreak of jungle yellow fever in Venezuela in 1929, after which the disease has been studied with great care, and continuously since the National Service for the Prevention of Yellow Fever in Venezuela was created in 1937. There are now 76 viscerotomy posts

operating. There are two endemic jungle yellow fever areas in Venezuela, both in the basins of the Maracaibo Lake and the Orinoco River. The first lies in the " Venezuelan Guiana," bounded by the Caroní River and the borders of the State of Bolívar with Brazil and British Guiana. This area is where the 1944–45 outbreak centred. The second is in the States of Táchira and Barina. There may be another focus at the northern watershed of the Andes towards Maracaibo Lake.

GAST and BATES (p. 644) compare the seasonal abundance of *Haemagogus capricorni* (the chief vector of yellow fever in eastern Colombia) with the seasonal distribution of human yellow fever in the region of Villavicencio. Briefly, it is recorded that in the post-dry season, increase in yellow fever lags about a month behind the increase in mosquitoes. Human yellow fever remains at a high level throughout the rest of the rainy season, even though mosquito populations are declining ; the peak of the disease in November and December corresponds to only a slight rise in mosquito population. The high incidence of yellow fever at this time is attributed to the local custom of felling large areas of forest in November and December : the human population is thus in closer contact with the forest in these months than at any other time.

POLAK (p. 264) in addition to making an extended summary of the literature on the epidemiology and control of yellow fever records that protection tests in Surinam indicate that jungle yellow fever exists there.

Aetiology.

LAEMMERT (p. 644) has studied the susceptibility of marsupials to different strains of yellow fever virus. Seven species were studied, which included 335 marsupials, mostly caught in areas of Brazil where yellow fever was epidemic or had been reported previously. Seven different strains of virus were used, mostly two S. American strains, J.Z. and O.C., which had been maintained in *rhesus* monkeys. The results are shown in detailed tables, and indicate that there was a varying susceptibility of the animals to the strains used. In particular, three species of opossum (*Didelphis marsupialis*, *D. paraguayensis* and *Metachirops opossum*) appeared to be resistant to the strains used, on the evidence of tests for circulating virus after inoculation. South American opossums are aplacental animals and the author thinks it unlikely that the newborn animals in the pouch acquire passive immunity from the mothers' milk.

The same writer, with DE CASTRO FERREIRA (p. 33) has isolated the virus on four occasions from wild marmosets, *Callithrix penicillata*, caught in the neighbourhood of Ilhéus, Bahia, where jungle yellow fever is endemic. All of them died with gross lesions of yellow fever, confirmed by animal experiments and histopathological examination. Examination of a further 1,437 marmosets proved negative. This is quoted as being the first isolation of yellow fever virus from naturally infected vertebrates other than man.

WADDELL (p. 214) has fed *A. aegypti* on marmosets or Cebus monkeys infected with jungle strains of yellow fever and tested them for virus content by intracerebral inoculation of mice.

The mosquitoes were killed either by chloroform, ether, potassium cyanide or tobacco smoke, and tested for virus content after various intervals.

After death from chloroform, most of the virus activity was lost in 30 minutes and was absent in one hour ; virus was recovered from the mosquitoes two hours after death by the other three methods, and was still present after 45½ hours in those killed by potassium cyanide, and in a similar period in *Aëdes aegypti* that had died of starvation.

Virus was recovered from *Haemagogus equinus* and *H. spegazzinii* 24, 48 and 72 hours after they had died spontaneously after feeding on infected

monkeys. The authors consider ether to be the most satisfactory agent for killing insects to be used for isolating yellow fever virus.

Transmission.

Bates and Roca-Garcia (p. 32) record the maintenance of a strain of yellow fever virus through five cycles in the laboratory, using (1) a Colombian strain of virus isolated from a patient who had died of the disease in an area north of Villavicencio, (2) wild-caught *Haemagogus capricorni* as vectors, (3) wild-caught Saimiri monkeys, whose serum had given negative protective tests. The results of intracerebral inoculation of the strain into adult white mice were variable, but 3- and 5-day old mice were very susceptible, as were Saimiri monkeys, 8 out of 10 of which died of acute yellow fever when infected by mosquito bite. Not all the mosquitoes became infected after feeding on infected monkeys, the percentage apparently being dependent on the quantity of virus ingested and the temperature at which the mosquitoes were kept. The extrinsic incubation period for *H. capricorni* was 22 to 24 days at 24° to 27°C. and 13 to 15 days at 30°C.

The authors believe that the relatively high temperature required for infection is obtained by the species frequenting sunny localities in the forest canopy, where temperatures are higher than in the lower strata ; also, the habits of the Saimiri monkeys in the Villavicencio area correspond closely with those of *Haemagogus*.

The same authors (p. 328) have carried out similar experiments, employing on this occasion four douroucoulis (*Aotus trivirgatus*) from the Villavicencio area. A local strain of yellow fever virus and the mosquito *H. capricorni* were again employed. All four animals developed acute fatal yellow fever, confirmed by all the usual tests. Virus was transmitted by the bite of *H. capricorni* from Saimiri to douroucouli, from douroucouli to douroucouli, and douroucouli to Saimiri. It is suggested, on the evidence, that douroucouli may be important in the epidemiology of yellow fever, as it is said to be the only monkey in certain endemic areas in Colombia.

Waddell and Taylor (p. 33) describe investigations of the cyclic transmission of yellow fever by alternate passage through insect vector and vertebrate host. Three virus strains were used, two Brazilian and one Colombian. Three series of experiments were carried out : (1) feeding *Aëdes aegypti* on a marmoset, *Callithrix aurita*, which had been infected with the virus, and subsequently on a normal marmoset. Nine cycles were maintained. All the marmosets became infected and showed virus on the 2nd or 3rd day ; 15 of 17 animals died on the 4th to the 8th day. The two which recovered showed virus up to the 4th and 5th days and were immune when tested on the 21st day. (2) Feeding *A. aegypti* on infected Cebus monkeys (*Cebus versutus*). Five cycles were maintained and all the monkeys showed circulating virus, but only one of 13 died. The remainder developed immunity. The concentration of virus in the circulation was low compared with that found in the marmoset. (3) Three cycles were completed with marmosets and *Haemagogus equinus*. Four successful transfers were obtained. In one experiment, three *H. spegazzinii* were able to transmit the virus from an infected to a normal marmoset. The experiments suggest that the virus may be preserved in forest areas by passage through sylvan mosquitoes and monkeys.

Haddow (p. 255) has studied the biting activities of *Aëdes simpsoni*, the vector of human yellow fever in Bwamba County, Uganda, and showed that it is a strictly diurnal species, most active on warm cloudy days. The principal local variety of raiding monkey is *Cercopithecus nictitans mpangae* Matschie. About half of those caught were immune to yellow fever and it is suggested that

an infected monkey feeding on bananas at a 12-ft. level could readily pass the virus to *A. simpsoni*.

Owing to the occurrence of two cases of yellow fever in Kenya at Kitale (1942) and Kisumu (1943) respectively, GARNHAM, HARPER and HIGHTON (p. 736) have investigated the mosquito position in the Kaimosi forest, between Kisumu and Kitale. The evidence accumulating as a result of catches producing 55 species of mosquitoes of ten genera, including known vectors of yellow fever, suggests that conditions in the Kaimosi forest are adequate for the establishment of yellow fever.

Immunity: clinical features.

SMITHBURN (p. 214) has studied the yellow fever protection test extensively and describes the final test adopted in Uganda. In this, 1 per cent. virus is used instead of the 10 per cent. used by Sawyer and Whitman. The details of the method are described. The high susceptibility of infant mice to intraperitoneal inoculation, and the possibility of enhancing this failing susceptibility in older mice by a preparatory intracerebral injection of starch solution is made use of in the test; also the use of younger mice means that less serum can be used than is necessary in standard tests with 6-week-old mice.

BUGHER (p. 215) has found that a number of yellow fever immune sera stored in glass ampoules at Yaba, Nigeria, under unfavourable conditions for 12 years, still contained demonstrable antibodies, although the average loss of protective power was about 50 per cent. per year. The velocity of deterioration seems to resemble that recorded by GLENNY for diphtheria antitoxin.

MACGRATH (p. 553) discusses two fatal cases of yellow fever in Europeans in West Africa, and describes autopsy findings.

Control.

SMITHBURN and MAHAFFY (p. 34) discuss the time of development and duration of immunity in monkeys and human beings as a result of immunization with the attenuated yellow fever virus 17D. In 12 rhesus monkeys, antibodies developed within 6 or 7 days but the monkeys were completely resistant at least 24 hours before the protective bodies appeared in the serum. Antibodies were present by the 10th day in most of ten human volunteers, and may be present on the 7th day. Post-vaccination immunity tests on persons in Africa inoculated with 17D vaccine showed that about 90 per cent. of those tested (soldiers and civilians in different parts of East Africa) showed protective antibodies after at least 22 to 36 months. Children responded equally with adults. FAVAREL (p. 329) has immunized guineapigs against yellow fever virus by cutaneous scarification. Seven of 11 guineapigs thus treated with the French strain of neurotropic yellow fever vaccine (218th mouse passage) were completely resistant 35 to 47 days later. On the other hand, all of 6 guineapigs vaccinated in the same way with culture virus 17D succumbed to yellow fever encephalitis when inoculated intracerebrally 25 to 50 days after scarification. The divergent results with the two strains may be explained as being due to the difference in neurotropism, and also on the assumption that one had a greater affinity for the skin of the guineapig.

In the Fourth Report of the Expert Commission on Quarantine, DE PAULA SOUZA (p. 1135) records an account of the controlled experiment to test the efficacy of the anti-yellow fever vaccine made at the Pasteur Institute at Dakar. Six hundred French soldiers were divided into 3 groups, receiving respectively (1) Dakar vaccine by scarification, (2) Dakar vaccine plus dry smallpox vaccine, by scarification, (3) Rockefeller 17D yellow fever vaccine subcutaneously. Tests were subsequently made and carefully controlled. The final results showed that about 98 per cent. of the first two groups and

about 65 per cent. of the third group had been immunized. Unvaccinated controls were negative in 29 out of 30 cases, and inconclusive in one. The Dakar vaccine was recommended by the Commission for approval.

The Commission also approved the yellow fever vaccine prepared at the South African Institute for Medical Research, Johannesburg, and approved this Institute and the Pasteur Institute at Dakar as institutes for testing the potency of yellow fever vaccine.

FREEMAN (p. 839) has made an epidemiological study of jaundice following yellow fever vaccination at a camp in the United States. Some 3·8 per cent. of the total average population at risk were hospitalized with jaundice. The average interval between vaccination and onset of epidemic jaundice was 12·3 weeks. The epidemic coincided with the large general epidemic among American troops in 1942. A large increase in the attack rate on the unvaccinated population was observed, and it is likely that all the cases of jaundice had a common aetiology, whether or not they had received yellow fever vaccine.

KAPLAN and GLUCK (p. 438) record the development of meningo-encephalitis in a 4½-year-old child who fell ill 5 days after vaccination by scarification with a neurotropic strain of yellow fever virus from the Pasteur Institute in Dakar. The virus could not be isolated from the cerebrospinal fluid, but the fluid gave positive protective tests. The child recovered completely, having improved suddenly in two or three days. The authors believe that inactive tissue culture virus should be used for vaccination if such accidents are to be avoided.

GAST-GALVIS (p. 924) describes the development and operation of the Colombia Viscerotomy Service, started in 1934. There are now 200 centres and 22,000 specimens have been taken. Changes of yellow fever were found in 352. The service has also proved of considerable value in the diagnosis of other diseases.

BEVIER (p. 1136) reports on yellow fever control in British Guiana. *Aëdes aegypti* control at the ports, and especially Georgetown, is well organized, and 207 persons are employed in the yellow fever service. There are 29,102 premises in the controlled areas. The working of the "premise breeding index" is described. Other control measures are discussed in detail. The roof gutter problem is costly, as dried *Aëdes aegypti* eggs cannot be destroyed by a blow-flame owing to the risk of fire, and because the local water supply depends very largely on roof collection by gutters.

Accounts are given of the use of insecticides, and larvivorous fish; the spraying of aircraft; and free vaccination. *H. J. O'D. Burke-Gaffney.*

MALARIA.

COVELL, G. **Malaria Course for Engineers at the Malaria Institute of India, Delhi. Opening Address.** *J. Malaria Inst. of India.* 1946, June, v. 6, No. 3, 317–20.

ALOSI, B. La malaria in Sicilia dopo cinque campagne antimalariche. [**Malaria in Sicily.**] *Riv. di Malariologia.* 1946, Feb., v. 25, No. 1, 19–30, 1 fig. English summary.

There was a marked increase of malaria in Sicily during the war. Continued bombardment caused a dispersion of urban populations; they found refuge in

small rural communities, where many contracted malaria. It was discovered that malaria was more widespread in certain parts of the Island than had been suspected. In the second year of the war the military forces in the Island were greatly increased. Among the arrivals were soldiers who had acquired malaria in Albania and Greece; they introduced fresh strains of malaria. The disease spread. Areas which had long been free from malaria became infected. In Messina, where no primary infections had occurred for many years past, fatal cases of pernicious malaria were reported. In 1944, 92 deaths were attributed to malaria in Sicily.

Agricultural methods, including primitive methods of irrigation, provide facilities for mosquito breeding. These require attention. Antilarval measures should be supplemented with the use of DDT against adult anophelines. There is a pressing need for medical centres in the most malarious parts of the Island. The free distribution of antimalarial drugs should be controlled so as to facilitate blood examinations. *Norman White.*

WILSON, D. Bagster. **Notes on the Epidemiology of Malaria in the East Africa Command.** *East African Med. J.* 1946, Sept., v. 23, No. 9, 258-72.

Tables embody the monthly incidence of malaria during the years 1943 to 1945 in European military staffs stationed in the following malaria-controlled places: Dar-es-Salaam (7° S. 39° E.), Port Reitz at Mombasa (4° S. 40° E.), Nairobi (1° S. 37° E.), Moshi (3° S. 37° E.), Lusaka (15° S. 28° E.), Zomba (15° S. 35° E.); they are based on hospital admissions. The following table summarizes the annual rates per 1,000 in those places in which figures were complete for each month of the year:—

Malaria Incidence (Rate per 1,000)—European Military Personnel

	1943	1944	1945*	Peak Months
Dar-es-Salaam: R.A.F.	1,061	596	183	May–June
Army	—	1,101	942	
Mombasa: R.A.F. (Port Reitz) ...	325	340	47	June–July
Army	267	459	55	
Nairobi	41	59	30	May–June
Moshi	—	—	285	March–June
Lusaka	—	—	344	Jan.–March
Zomba	—	—	724	March–May

*Mepacrine introduced in certain areas.

A second series of tables for the same places give the available figures of "average house catches of vector *Anopheles*" per month at central and peripheral catching stations in the "controlled" areas, during the years 1942 to 1945; figures for 1945 are given for adjacent "uncontrolled" areas. The author claims that standard methods have been followed in the recording of anopheline infestation in houses over three or four years; the method was "weekly hand catches in selected native houses carried out by means of torches and test tubes," the minimum period for a single searcher at each house being 30 minutes.

The following table is an extract from the above series :—

Average House Catches of Vector Anopheles

		Controlled Central Stations			Uncontrolled
		1943	1944	1945	1945
Annual Mean :	Dar-es-Salaam	1·17	1·47	0·38	8·50
	Port Reitz (Mombasa) ...	—	0·10	0·03	13·6
	Nairobi	0·08	0·11	0·03	—
	Moshi	—	—	0·33	1·0
April to July :	Dar-es-Salaam	2·55	3·95	0·67	14·2
	Port Reitz (Mombasa) ...	—	0·37	0·11	17·4
	Nairobi	0·17	0·21	0·04	0·32
	Moshi	—	—	0·80	0·92

The vector mosquitoes are *Anopheles gambiae* and *Anopheles funestus* ; in the coastal places over 80 per cent. of catches were *Anopheles gambiae.*

The author concludes that while anopheline control [detail not referred to] may be very effective in controlling malaria for the greater part of the year, an efficient larval control may fail to check the high seasonal incidence caused by *A. gambiae* in the more intensely malarious parts of East Africa ; effective control demands the reduction of Anopheles by 99 per cent. in such areas.

Six thousand feet in the Nairobi area is quoted as the critical height above which *A. gambiae* cannot survive in dangerous density.

[Drs. J. G. S. TURNER and G. A. WALTON in their Departmental Report on Malaria in Freetown (8° N. 14° W.), where the vector mosquitoes are *A. gambiae* and *A. melas*, quote the probable incidence of malaria in the army in 1940 to have been 6,000 per 1,000 per annum ; the steady and progressive application of modern control measures (including mepacrine in 1944) reduced the incidence to 73 per 1,000 per annum in 1944.] *R. Ford Tredre.*

ZAMENLOF, J. **Malaria at Kidugala Polish Refugee Camp, Tanganyika.** *East African Med. J.* 1946, Oct., v. 23, No. 10, 311–17.

DE BURCA, B. **Tropical Zone Malaria associated with an Increase in** *P. falciparum* **Infections in the Spring Wave.** *J. Malaria Inst. of India.* 1946, June, v. 6, No. 3, 265–7, 1 graph.

" An account is given of a spring wave of malaria occurring in Central India associated with a definite increase in M.T. infections and accompanied by considerable mortality.

" No investigations were carried out to establish the vector but dissection results immediately north of the area involved indicate that *A. culicifacies* may be responsible. A brief account of a spring wave on the coast of Eritrea occurring in an area where there is no autumnal wave is also given."

YACOB, M. & SWAROOP, S. **Malaria and Rainfall in the Punjab.** *J. Malaria Inst. of India.* 1946, June, v. 6, No. 3, 273–84, 1 chart & 2 maps.

" The relationship between rainfall and malaria has been studied by correlating the rainfall data with the epidemic figure. High and statistically significant coefficients of correlation have been obtained.

" Correlation has been studied separately on the rainfall figure of each month. A hitherto unrecognized relation is the correlation of the May rainfall with the epidemic figure. It seems possible that this relationship may

enable a preliminary forecast of the probable malaria incidence to be issued some three months earlier than at present.

"The variation in the degree of association amongst different districts and also from month to month is discussed."

FAUST, E. C., HESS, A. D. & YOUNG, M. D. **Malaria Mortality and Morbidity in the United States for the Year 1944.** *J. National Malaria Soc.* Tallahassee, Fla. 1946, June, v. 5, No. 2, 103–12. [15 refs.]

FORBES, L. S. D. & CODA, D. Casos de malaria importados de um pôrto Africano. [**Cases of Malaria imported from an African Port.**] *Arquivos de Hig. e Saúde Pública.* São Paulo. 1945, Sept., v. 10, No. 25, 83–6. English summary.

A steamship arrived in Santos after a 14 days voyage from Freetown with 14 per cent. of the crew suffering from primary *P. falciparum* malaria. For 6 days the ship had been anchored in the bay at Freetown, a mile or so from the shore. With the memory of the serious results arising from the introduction of *A. gambiae* from Africa into Brazil the authors insist on the importance of measures which all ships entering malarious ports should take to prevent the ingress of anophelines aboard. They consider, too, that in such cases drug prophylaxis for the crew should be compulsory. *Norman White.*

CHRISTOPHERS, S. R. **Some Remarks on the Nomenclature of the Malaria Parasites of Man.** *Rev. Inst. Salubridad y Enfermedades Trop.* 1945, Dec., v. 6, No. 4, 213–27.

In this paper the author returns to the subject of the nomenclature of the three common malarial parasites of man which he discussed in an earlier paper with SINTON and upon which SABROSKY and USINGER also made comments [this *Bulletin*, 1939, v. 36, 390, and 1945, v. 42, 244]. In the present paper the author gives a list of the generic synonyms of *Oscillaria* Laveran with type species, references and notes, a second similar list of the species synonyms and a third list of relevant references in chronological order. The discussion shows finally that the names most generally employed at the present time are, according to the Rules of Nomenclature, incorrect, that the utmost confusion would result if attempts were made to introduce the correct names and that the only satisfactory procedure is for the International Commission to suspend the rules in order to validate the names commonly in use. *C. M. Wenyon.*

HUFF, C. G. **A Consideration of the Problem of Evolution of Malarial Parasites.** *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1945, Dec., v. 6, No. 4, 253–8.

The author discusses the origin of malarial parasites and their allies and thinks it possible that they were originally parasites of Diptera which became adapted to reptiles, owing to invasion of the salivary glands by sporozoites, and later to birds and mammals. He admits that the suggestions are highly speculative and that further knowledge of the life-histories of these parasites

in various hosts, particularly lizards, is needed before any probable evolutionary scheme can be enunciated. *C. M. Wenyon.*

OBERLÉ, G. Recherches sur les formes extraérythrocytaires du paludisme humain à *P. vivax.* [**Exoerythrocytic Forms of** *P. vivax* **Malaria in Man.**] *Bull. Soc. Path. Exot.* 1945, v. 38, Nos. 1/2, 27–37, 5 figs. [29 refs.]

The author has examined the bone marrow by sternal puncture in five cases of general paralysis during malarial therapy. The infections were induced by blood inoculation of a strain of *P. vivax.* Sternal puncture was performed the day before subcutaneous injection of infective blood (10 cc.) or intrasternal inoculation of infective bone marrow (3 cc.). It was again performed on the 5th day after inoculation and every two or three days until on thick film examination parasites appeared in the blood, which event occurred two or three days before any febrile reaction was evident. Another puncture was carried out during the 8 or 10 bouts of fever which were permitted to take place and again after treatment had banished all parasites from the blood. Though many films of the material obtained by the various sternal punctures were carefully examined for exoerythrocytic stages of development, in only one instance in one of the cases was a signet ring type of parasite seen in a reticulo-endothelial cell on the 5th day after inoculation. On the other hand, in all the cases extracellular non-pigmented parasites were seen from the 5th day onwards. They were not seen at the last attack of fever, nor after treatment. For some time they co-existed with the pigmented erythrocytic forms. The types of extracellular parasites were ring forms measuring 2μ in diameter up to larger forms with seven chromatin bodies. The author notes that most of the previous records of exoerythrocytic development in human malaria have been in cases infected by sporozoites. The results of his observations lead him to the conclusion that they occur just as frequently after the inoculation of infective blood. A criticism has been made that in such cases the inoculated blood may have contained undetected exoerythrocytic stages or their merozoites of sporozoite origin. This can hardly apply in this case, where the strain of parasite used had been subjected to blood passage only for 21 years. The author points out that in the marrow smears, in addition to the undoubted parasites, there occur also fragments of the cytoplasm of granular cells which, though having some resemblance to the schizonts, can be distinguished by their different staining reactions. He discusses the bearing of his results on the observations of earlier observers up to the time of the presentation of his paper (July 12, 1944). He mentions an interesting observation of COUDERT and EYQUEM (*J. Méd. de Lyon,* 1944, No. 584, 305) that on the 5th day after inoculation of parasites the sternal marrow contained only endohistiocytic forms, while at the same time the blood contained no erythrocytic stages and was not infective on inoculation. The author himself has found that the marrow containing only extracellular forms was infective, though erythrocytic forms first appeared in the blood five days later.

[In connexion with the discovery of non-pigmented stages of malarial parasites it is perhaps well to remember that when erythrocytic pigmented schizonts liberate their merozoites these are for a while extracellular non-pigmented stages. Of these merozoites only a small percentage gain entrance to erythrocytes. The remainder are subjected to phagocytosis. It is evident therefore that small non-pigmented stages are liable to be found in smears of organs both extracellularly and within phagocytic cells. It also seems possible that the phagocyted parasites might undergo some development before being finally destroyed, particularly when the phagocyte is a reticulo-endothelial cell.] *C. M. Wenyon.*

LANZA, G. Documentazione di forme istotrope del parassita malarico nell'uomo. [**Documentation of Exoerythrocytic Forms of the Malarial Parasite in Man.**] *Pathologica.* 1944, Jan.–Dec., v. 36, No. 627, 24–7. [12 refs.] English summary (9 lines).

The author discusses the various claims which have been made to the discovery of exoerythrocytic stages of development in human malaria, and reaches the conclusion that there is no satisfactory evidence that these correspond with the definite stages which have been found in the case of bird malarial parasites such as *P. gallinaceum.* In most cases they have been seen in smears of bone marrow in which fragments of the cytoplasm of damaged cells will frequently contain a single red granule or a number of such, producing very good imitations of the exoerythrocytic forms of bird malarial parasites. Furthermore, the histiocytes possess certain phagocytic powers which lead them to ingest various bodies, including cell detritus, pigment and liberated malaria parasites, which, undergoing dissolution, may assume forms which might be thought to be pigment-free exoerythrocytic stages of development.

In an investigation of 15 cases of malaria the author found scanty extracellular pigment-free forms in the bone marrow of two cases of *P. vivax* infection and one case of *P. falciparum* infection. In one case of severe *P. falciparum* infection, he found in the spleen numerous small pigment-free parasites within the histiocytes. They were present in some cells in such numbers as to produce a resemblance to a leishmania infection. In this case the abundance of pigment-free parasites contrasted very markedly with the usual extreme scarcity of parasites in the internal organs of malarial subjects. While admitting that pigment-free forms may occur and that in certain cases of pernicious malaria they may be present in cells of the reticulo-endothelial system in large numbers, the author holds that this reveals merely a reticulo-endothelial tropism of the malarial parasite, which is no proof that an obligatory endothelial developmental phase precedes the erythrocytic stages of development after the injection of sporozoites.

[For the information of those who read only the summaries to the paper, in those in English and German the forms found in the three cases are erroneously referred to as pigmented forms.] *C. M. Wenyon.*

BELTRÁN, E. & SANDOVAL, A. M. Infección de reticulocitos por *Plasmodium vivax* en la sangre periférica y la medula esternal. [*P. vivax* **Infection of Reticulocytes in the Sternal Marrow and the Peripheral Blood.**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1945, Dec., v. 6, No. 4, 195–8. English summary.

In ten cases of general paralysis treated by induced *P. vivax* infection, the authors have counted the percentage of reticulocytes in the bone marrow and peripheral blood. In the marrow the percentage varied from 0·8 to 2·5, while in the blood it varied from 0·4 to 2·1. Among red blood corpuscles infected with ring stages of the parasite, 15 to 90 per cent. were reticulocytes, giving an average of 41·8 per cent., a figure which indicates clearly that the merozoites show a preference for reticulocytes. *C. M. Wenyon.*

YOFE, J. & FOX, D. G. R. **The Behaviour and Feeding Habits of Anopheline Mosquitoes.** *J. Trop. Med. & Hyg.* 1946, Oct.–Nov., v. 49, No. 5, 88–91, 3 figs.

Any ecological survey is intended to enable an accurate picture of some feature of the animal or plant population to be drawn. Some of the early

attempts to assess the true density of mosquitoes, and their relation to malaria, gave confusing results as the different reactions of the various species were not sufficiently understood.

In central Burma 12 species of *Anopheles* were found, and of these, three, *viz. A. aconitus, A. philippinensis* and *A. minimus,* were found in considerable numbers. In a series of trapping experiments carried out between November 2nd and December 17th, 1945, some 40,000 anopheline adults were collected and identified.

Two cattle in a shed were used as bait and catching was carried out nightly from 19.00 to 23.00 hours. No other animals or human habitations were situated within 80 yards. There was considerable fluctuation in the catch from night to night, but the same approximate proportion of the different species was maintained, *A. aconitus* made up 58 per cent. of the catch, *A. philippinensis,* 31 per cent., and the remaining ten species only 11 per cent., of which *A. minimus* was less than 0·5 per cent.

Catches were then made in a native hut containing several men. The total catch was smaller, but the ratio of the species was quite different. *A. minimus* made up 63 per cent. of the total, *A. aconitus* 21 per cent. and *A. philippinensis* 11 per cent. In this case, a cattle shed nearby gave a similar ratio to the previous collection (*i.e. A. aconitus* vastly predominating).

A further analysis of the results, and a study of the resting habits of the insects, made it clear that *A. minimus* was attracted by man and hardly at all by animals, while *A. aconitus* and *A. philippinensis* were almost entirely animal feeders. It is suggested that these last two can only be of negligible importance in transmitting malaria, for even if a few with sporozoites are found they are unlikely to feed twice on man during their lifetime. The close relation between *A. minimus* and man was further stressed by daytime collections of resting mosquitoes in huts ; this species made up 93 per cent. of the total.

Kenneth Mellanby.

BURGESS, R. W. & YOUNG, M. D. **Experimental Transmission of** *P. falciparum* **by** *Anopheles maculipennis freeborni. J. National Malaria Soc.* Tallahassee, Fla. 1946, June, v. 5, No. 2, 151–2.

KRIVONOSOVA, Z. F. [**The Output of** *Anopheles plumbeus* **Steph. in Tree-Holes.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1946, v. 15, No. 1, 42–3. [In Russian.]

In order to determine the number of *Anopheles plumbeus* produced from the hole of a tree, the author selected one in which the water covered an area of 1,000 sq. cm. and contained numerous larvae. The hole was covered with a muslin hood and every other day all the imagines which had emerged were captured. During a period of two months the author caught 170 female and 131 male *A. plumbeus* and 31 *Aëdes geniculatus,* a total of 332 mosquitoes in 60 days, *i.e.* on the average 5·5 per day. In another experiment the water in a hole having a surface area of 125 sq. cm. was "seeded" with 100 eggs, of which 88 produced adult mosquitoes. The author considers these figures to be of epidemiological importance in assessing the rôle of this mosquito as a vector of malaria.

C. A. Hoare.

IVANOVA, L. V. [**Peculiarities of Behaviour of** *Anopheles plumbeus* **Larvae in Connexion with Conditions in its Habitat.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1946, v. 15, No. 1, 30–40, 8 figs. [In Russian.]

The author describes observations and experiments carried out with the larvae of *Anopheles plumbeus* obtained from tree-holes in the Caucasus and

kept in the original water in Moscow. The breeding places in tree-holes represent small, shallow water collections which are heavily shaded, devoid of vegetation, and in which peculiar chemical conditions obtain, while the daily variation of temperature is slight. It was natural to expect to find certain peculiarities in the behaviour of animals living under such ecological conditions. The behaviour of the larvae of *A. plumbeus* is compared with that of *A. maculipennis*, which the author had previously described. While in the latter species the descent and rise of the larvae is accompanied by gliding, in the former species there is no need for rest, in view of the shallowness of the water, and the movements are accordingly not interrupted by gliding. In connexion with this, the hairy covering of *A. plumbeus* is less developed than that of *A. maculipennis*. Since the surface of the water in tree-holes is undisturbed, the larvae of *A. plumbeus* do not have to anchor themselves, and the morphological adaptation serving this purpose, *i.e.* the hooks of the caudal hairs, are consequently rudimentary, whereas the larvae of *A. maculipennis*, in which the reaction of stereokinesis is pronounced, have well developed hooks. The larvae of *A. plumbeus* manifest a strong negative phototaxis and an increased photokinetic reaction.

Immediately on exposure to light, the larvae try to escape from it, but when the stimulus is prolonged they react by erratic movements, irrespective of the source of light. These reactions enable the larvae of *A. plumbeus* to hide in the darkest corners of the tree-hole. *C. A. Hoare.*

ULITCHEVA, A. V. [**The Quantitative Evaluation of *Anopheles* Production in Typical Breeding Places and its Epidemiological Significance.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1946, v. 15, No. 1, 25–9. [In Russian.]

The author describes the results of an assessment of the epidemiological significance in malaria of various types of water-collections. This study was based on a quantitative estimate of the following data : the density of anopheline pupae per unit of area, the total anopheline-bearing area of water-collections of each type, and the temperature of the water in relation to the rate of development of the anopheline mosquitoes. The observations were carried out from June to September, in the Urgut district of Uzbekistan, where mosquito-breeding takes place in swamps, rice-fields and swampy pools.

The total output of mosquitoes (*Anopheles sacharovi* and *A. superpictus*) for each type of water-collection per month was determined from the formula $P=\frac{A.S.}{Q}n$, in which P=anopheline production of the breeding-place ; A=mean daily density of pupae per 1 hectare ; S=area of each type of water-collection ; Q=duration of development of pupa (according to Bodenheimer's formula) ; n=number of days in a month during which observations were made.

From these observations, the results of which are set out in seven tables, it is seen that the proportion of mosquitoes bred in water-collections of different types was as follows : 24 per cent. in swamps with a mean area of about 40 hectares ; 71 per cent. in rice fields (mean area 8 hectares) ; 5 per cent. in swampy pools (mean area 2·2 hectares).

The mosquito output of each type of water-collection varies with the season : in spring, the chief breeding places are the swamps, which are responsible for 100 per cent. of the mosquitoes emerging during that period, while in summer 80 per cent. of the mosquitoes are produced in rice-fields. On the basis of the evaluation of the mosquito-output for each type of breeding place in different

seasons, it is possible to determine the type of water-collection in a given locality which serves as a focus of malaria and is responsible for outbreaks during the second half of the summer. *C. A. Hoare.*

ETHERINGTON, D., HICKLING, S., RODEN, A. T. & SELLICK, G. **Malaria Transmission by Unusual Vectors in Northern Italy.** *Riv. di Malariologia.* 1946, Feb., v. 25, No. 1, 1–12.

The observations recorded relate to the psychiatric hospital about two kilometres south-west of the town of Vercelli. The Province of Vercelli is in the western half of the middle Po valley. In the nineteenth century it was highly malarious, but thereafter malaria incidence steadily declined. No case was recorded from 1912 to 1918, and only very few sporadic cases until 1943. In July 1943, cases of malaria began to occur among patients at the psychiatric hospital, who had not received malaria therapy, and among members of the staff. Cases occurred in the two subsequent years: 51 primary cases were reported in August 1945, the highest monthly total during the three years. All the infections were with *P. vivax*. During 1941 and 1942 patients requiring malaria therapy were infected by *A. maculipennis* which had been infected with *P. vivax* at the Rome Institute of Malariology. Thus a reservoir of infection was created. Mosquito screening had fallen into disrepair.

The predominant anopheline in this area is *A. maculipennis* var. *messeae*. *A. m. melanoon* also occurs. *A. hyrcanus* (*pseudopictus*) was as plentiful as *A. maculipennis* in stables in August, but the latter predominated in the hospital buildings. All these mosquitoes are generally considered to be of no importance in the transmission of malaria in Italy, where they are normally zoophilic. Mosquitoes dissected numbered 519. Sporozoites were found in one of 113 *A. hyrcanus* and in 1 of 72 *A. m. messeae* dissected in August 1945. *Norman White.*

AKALIN, M. S. Anofeles Makülipenis Varyete Singaref ve Anadolu Makülipenis'leri eihazi tenasülilerinde görülen anomaliler. [**Morphological Anomalies in** *Anopheles maculipennis.*] *Türkische Ztschr. f. Hyg. u. Exper. Biol.* Ankara. 1941, v. 2, No. 2, 128–38. German summary 139–41, 6 figs.

In Turkey *Anopheles maculipennis* seems to produce anomalous varieties in male genitalia. The parabasal spines in the male genitalia (which should be three) may be any number from one to five, and are frequently different on the two sides of the body. Several types are figured. The commonest has three on each side, but specimens with two on each side made up 13 per cent. [presumably of all males examined]. The paper contains a number of crude figures of eggs, some of them referable to well-known races. To what race the anomalous males belong is not stated in the legends to figures, nor in the brief German summary. [The bulk of the paper is in Turkish. The German translation of the heading of the table contains at least one error.] It may well be that the author has made an interesting discovery. *P. A. Buxton.*

VINCKE, I. Note sur la biologie de *Anopheles dureni* Edw. [**The Biology of** *Anopheles dureni.*] *Ann. Soc. Belge de Méd. Trop.* 1946, June 30, v. 26, No. 2, 161–74, 2 figs.

The collecting of anophelines near Elizabethville, Belgian Congo, from January 1944 to December 1945, has shown that *Anopheles dureni* has a strictly limited range in this area, apparently confined to the trees near its breeding place in the Kisanga river. Repeated searches in huts, houses, stables and the like failed to

produce this species but in the open, among adults of 14 species of Anopheles collected, *A. dureni* formed 51·78 per cent. and *A. implexus* 40·52 per cent. From the nearby river larvae of eleven species were taken, 43·03 per cent. of which were those of *A. dureni*.

Seven hundred and thirty-three females dissected between January 1944 and January 1946 produced a sporozoite index of 7 per cent., but during February to April 1946, only four out of 83 examined contained human blood ; during the same period 23 out of 25 *A. funestus*, 10 out of 10 *A. gambiae*, and 14 out of 14 *A. implexus* were positive for human blood.

Investigations are continuing in order to identify the *Plasmodium* and to determine whether it is transmitted to man by *A. dureni*.

A table gives the numbers of trees examined month by month for the two years and the numbers of *A. dureni* collected from them. Charts show the seasonal distribution of the adults and larvae, from which the period of greatest prevalence is seen to be from November to March. *H. S. Leeson.*

WOLFS, J. Sur les anopheles de l'agglomération de Coquilhatville et sur leur rôle respectif dans la transmission du paludisme dans cette agglomération. [**The Anopheles of Coquilhatville and their respective Rôles in the local Transmission of Malaria.**] *Ann. Soc. Belge de Méd. Trop.* 1945, Dec. 31, v. 25, Nos. 3/4, 225–30.

Coquilhatville is on the Equator and is surrounded on the north and north-west by the Congo, on the north-east by the Congo's great tributary the Ruki, and on the other sides by tree-covered swamp. The banks are high where the rivers join but further up the Ruki the bank is a vast grassy marsh, subject to flooding, the floods reaching a part of the European settlement. There are numerous islands in both rivers.

Nine species of *Anopheles* were found in Coquilhatville and adjacent villages (the numbers of adults captured in 1944 are indicated) : *A. moucheti* 8,000 ; *A. paludis* 7,000 ; *A. obscurus* 300 ; *A. concolor* 40 ; *A. gambiae* 30 ; *A. implexus* var. *henrardi* 20 ; *A. nili* 5 ; *A. coustani* 2 ; and *A. funestus* 1. It is interesting to note that *A. gambiae*, the most prevalent species in the Congo generally, here takes only fifth place. *A. moucheti* is widespread in European and native quarters. *A. paludis* and *A. obscurus* are found in greater numbers in the verandahs than in the interior of houses. *A. concolor* was only taken outside houses near the river. *A. gambiae*, which is very rare, was found in the native city and in two villages. *A. implexus* var *henrardi* is a new variety that was found on tree trunks near the river bank. *A. implexus* type is a mosquito of the high regions of Elisabethville and Ruanda-Urundi ; it has never been found in the central basin of the Congo. The other three species were so rare as to be negligible.

The capture of larvae showed a curiously dissimilar distribution of species. *A. paludis* was found breeding in great numbers and in most diverse places near the European quarters and elsewhere, but the only breeding places of *A. moucheti* found were in islands in the river opposite the port among flooded high grass. The explanation of its great prevalence as an adult remains to be solved. *A. gambiae* was more commonly found in larval than in adult form, but only outside the town, and even here full-grown larvae were rare. A possible explanation is that a stratum of limonite [Bog-ore] lies very near the surface and casual collections of water, such as those in which *A. gambiae* often breed, are commonly covered with a layer of iron, looking like a film of oil.

Endemic malaria is much less severe in Coquilhatville than in other large Congo agglomerations. *A. moucheti* is probably the most important local

vector: the author dissected 1,500; the sporozoite index was only 0·86 per cent. *A. paludis* is not a vector as a general rule; only one specimen with sporozoites was found among several hundred dissected. *Norman White.*

MORTIMER, D. A. **Notes on the Anopheline Fauna of Manipur Area, Eastern Assam.** *J. Malaria Inst. of India.* 1946, June, v. 6, No. 3, 269–71.

SCHIAVI, A. Nota sôbre mosquitos vetores em Iguape. [**Note on the Mosquito Vectors in Iguape.**] *Arquivos de Hig. e Saúde Pública.* São Paulo. 1945, Sept., v. 10, No. 25, 69–75, 1 map. English summary (5 lines).

The town of Iguape lies in the delta of the Ribeira River. Its southern side is separated from an island, Ilha Comprida, by a strait, Mar Pequeno, some one and a half kilometers wide. The southern shore of the narrow island borders the Atlantic. Iguape suffers from sometimes severe endemic malaria: 8 to 10 per cent. of the population suffer annually, 4 to 7 per cent. from primary infections. The infection rate of females was nearly three times higher than that of males. The author made an incomplete survey in the early months of 1944; January was the month of maximum malaria incidence. He found *A.* (*N*) *albitarsis domesticus* to be the most prevalent anopheline and it is considered to be the most important vector. Of 107 adults collected 89 were of that species, 10 *A. intermedius*, 1 *A. oswaldoi*, 1 *A. mediopunctatus*, 2 *A. cruzi* and 4 *A. belator*. Of 60 *A. albitarsis domesticus* dissected five were found with oöcysts; two of these also had sporozoites. The infection rate was thus 8·3 per cent. This mosquito was very much more prevalent in parts of Iguape bordering the Mar Pequeno than elsewhere and evidence is produced which indicates that the chief breeding grounds are in the Ilha Comprida, one and a half to two kilometers distant. *Norman White.*

RACHOU, R. G. Da domesticidade dos anofelinos do sub-genero *Kerteszia* no litoral do Estado de Santa Catarina. [**Domesticity of the Anopheline Sub-Genus *Kerteszia* in Santa Catharina, Brazil.**] *Folha Med.* 1946, July 25, v. 27, No. 14, 105–7. [Summary in English by the author.]

"The anophelines of the sub-genus *Kerteszia*, represented by three species——*cruzi*, *bellator* and *homunculus* (?)—had been found naturally infected in several localities of the State of Santa Catharina (south of Brasil), where they invade houses in a very high density. The author gives the result of some observations in this region about domestic habits of these anophelines. In 1944, among 15,265 anophelines captured indoors, 15,205 (99·5 per cent.) were identified as *Kerteszias*. Thirteen localities had been studied; five of them presented a relative incidence of 100 per cent. of *Kerteszia* in the houses; this incidence had oscillated between 89·1 per cent. and 99·8 per cent. in the others.

"Realizing four captures in a house, of 96 hours each one, the author collected 8,949 specimens of *Kerteszia*. These mosquitoes entered the house at any hour of the day or of the night, more at night than at day-time. During the night their entrance was more active, between mid-night and 6.00 P.M. [*sic:* ? A.M.] The hour with the highest density of mosquitoes was 5.00–6.00 P.M. [*sic:* ? A.M.], presenting a median density of 66·94."

RACHOU, R. G. O *Herpetomonas pessoai* Galvão e Coutinho, 1941 parasitando o *A.* (*K.*) *cruzi* Dyar e Knab, 1908. [*Herpetomonas pessoai* **as a Parasite of** *Anopheles* (*K.*) *cruzi.*] *Folha Med.* 1946, July 25, v. 27, No. 14, 112. [Summary in English by the author.]

"At Caldas da Imperatriz, Santa Catarina, dissecting 292 anophelines of the species *A.* (*K.*) *cruzi*, the author found 8 (2·7 per cent) specimens with their

stomachs parasited by flagellates, that were identified by Dr. J. O. Coutinho as *Herpetomonas pessoai* Galvão & Coutinho, 1941. Among these 8 parasited *A.* (*K.*) *cruzi*, 2 laid eggs and 1 presented oocysts of *Plasmodium sp.*, while Galvão and Coutinho, when they described the *H. pessoai*, admitted a probable pathogenic action of the species, represented by the lack of development of the ovaries and the friability of the stomachs of the infected mosquitoes observed by them."

KEAN, B. H. & TAYLOR, C. E. **Medical Shock in the Pathogenesis of Algid Malaria.** *Amer. J. Trop. Med.* 1946, Mar., v. 26, No. 2, 209–19, 2 charts. [23 refs.]

The authors describe six cases of *P. falciparum* malaria in which algid symptoms developed. The clinical findings were those of medical shock, including lowered blood pressure and other signs of vasomotor collapse. There was evidence of haemoconcentration. All the patients responded to replacement therapy : plasma in three cases, whole blood transfusion in one, and intravenous fluids in five. Oxygen was administered in two cases, " Eschatin " in two, and epinephrine in five.

The essential feature in shock is the disparity between the volume of the circulating blood and the size of the vascular bed. This may be produced by neurogenic, vasogenic or haematogenic factors. In the cases reported the shock appeared to be mainly haematogenic. Depletion of the volume of the circulating blood in malaria may be caused by the loss of water and electrolytes by vomiting, diarrhoea and diaphoresis. The haemolysis of red cells may be equivalent to the loss of whole blood through haemorrhage. In the cases reported the degree of parasitization was not unduly high and anaemia was slight. Haemoconcentration early in the development of the shock syndrome suggests that the loss of plasma, by damage to capillary walls by the action of haemolysed red cell constituents, is the initiating factor. The concept that algid malaria is due to the development of medical shock suggests appropriate treatment ; specific treatment of the malaria infection must be vigorously continued while appropriate supportive measures are being applied. *Norman White.*

LIPPINCOTT, S. W., MARBLE, A., ELLERBROOK, L. D., HESSELBROCK, W. B., ENGSTROM, W. W. & GORDON, H. H. **Liver Function Tests in Neurosyphilitic Patients with Induced Vivax Malaria of Pacific and Mediterranean Origin.** *J. Lab. & Clin. Med.* 1946, Sept., v. 31, No. 9, 991–8.

The investigation deals with liver function tests in 138 neurosyphilitic patients who had previously received a course of drug treatment and none of whom had any evidence of hepatic disease. Complete tests were made on a number of these patients previous to, during, and after malarial fever caused by infection with *P. vivax* of Mediterranean or Pacific origin, through blood or sporozoite inoculation. Quinacrine (atebrin, mepacrine) was used to terminate the fever after 8 to 14 paroxysms, when approximately three weeks of parasitaemia had been experienced. The authors' methods have been given previously [this *Bulletin*, 1946, v. 43, 523]. It was then shown that only mild transient disturbances of liver function resulted from natural infections with *P. vivax* from the Pacific. Studies on similar lines to the present have been reviewed in this *Bulletin* [1943, v. 40, 582 ; 1945, v. 42, 341 ; 1946, v. 43, 97], and very recently those of GLENN *et al.* [below]. In the dye-retention and cephalin flocculation tests the present authors found that abnormal values predominated during the period of fever. Normal results were obtained in the galactose tolerance tests and those for the intravenous hippuric acid test were abnormal in only a small percentage of patients. During fever and for a

short time thereafter the values for icterus index, serum bilirubin and urinary urobilinogen were increased in some patients. These laboratory tests were correlated with clinical findings, and hepatic enlargement, accompanied in some cases by tenderness of the organ, was noted in a large percentage of patients. A prominent feature was nausea and vomiting, and a small percentage of patients had jaundice with signs of acute hepatitis. The general conclusion of the authors was that while some liver dysfunction was apparent during malarial therapy in the majority of patients, in the two months following termination of fever by quinacrine the organ functioned in the same way as before therapy was started. *J. D. Fulton.*

ARIETI, S. **Histopathologic Changes in Cerebral Malaria and their relation to Psychotic Sequels.** *Arch. Neurology & Psychiatry.* 1946, July, v. 56, No. 1, 79–104, 11 figs. (1 coloured). [Refs. in footnotes.]

GLENN, P. M., KAPLAN, L. I., READ, H. S. & BECKER, F. T. **Clinical and Laboratory Studies of Liver Function in Therapeutic Malaria.** *Amer. J. Med. Sci.* 1946, Aug., v. 212, No. 2, 197–206.

Earlier studies on liver function in malaria have been reviewed in this *Bulletin*, 1943, v. 40, 582 ; 1945, v. 42, 341 ; 1946, v. 43, 97. The authors' interest in the subject was aroused by the occurrence of jaundice in neurosyphilitic patients undergoing malaria therapy, and the value of certain diets in hepatitis has now been investigated by them. The patients, sixty in all, were soldiers, mostly young and in good health, who had been receiving mapharsen and bismuth treatment for some months. The skins of some were still slightly coloured from the use of suppressive atebrin when the experiments began. Clinical and laboratory observations were made previous to infection with *P. vivax* or *P. malariae* and subsequently until discharge ; they included estimations of haemoglobin, icterus indices, plasma proteins, urinary urobilinogen and hippuric acid excretion, cephalin-cholesterol flocculation tests, prothrombin times and van den Bergh reactions.

The patients were divided into three groups at random, 15 in each group being infected with *P. vivax* and five with *P. malariae*. Negro patients were infected only with the latter. One group received routine treatment only, while a second group was given extra protein and tablets containing vitamins A, members of the B group, C and D, together with injections of liver extract. The diet of the third group was similar to that of the second, but intravenous glucose containing ascorbic acid and thiamin was given in addition. Detailed clinical records were made of all patients. The malaria in the second and third groups appeared to be more severe than in the first, as judged by the usual criteria. Complications, apart from liver upset, were approximately equal in all three groups. The slight scleral jaundice noted in each group was not correlated with the presence of palpable livers, and judged by this criterion there was least involvement of this organ in the third group. Digestive symptoms, which were most pronounced in the first group, also appeared to be unconnected with liver enlargement. The administration of atebrin and mapharsen at the end of each course of treatment caused enlargement of this organ. The values of the icterus indices and van den Bergh reactions were similar in all three groups and slight oedema was encountered in each. High bilirubin levels in blood were not correlated with liver enlargement but appeared to be associated with anorexia. Estimation of plasma proteins showed the usual decrease at the time of fever, with alteration in albumin/globulin ratios, which soon returned to normal in all three groups. Hippuric acid excretion was also similar in the three groups and was lowered when atebrin and mapharsen were given. Judged by the

cephalin flocculation tests, there was a slow return of normal liver function after malaria. Urinary urobilinogen tests yielded no information of special interest. The pathological findings in two fatal cases indicated liver damage. The results of the above tests point to some degree of liver dysfunction in malaria, especially with regard to detoxication. The organ was apparently not protected by excess protein or vitamin intake, or by injections of liver extract; but intravenous administration of 75 gm. glucose daily had a marked effect in preventing liver enlargement. *J. D. Fulton.*

LANZA, G. Citologia del midollo osseo nella malaria acuta. [**Cytology of Bone Marrow in Acute Malaria.**] *Pathologica.* 1944, Jan.–Dec., v. 36, No. 627, 31–7. [13 refs.] English summary (9 lines).

The author has studied the sternal bone marrow in 15 cases of malaria. He sets out his findings in a comprehensive table. The cases show an increase in the reticulo-endothelial and plasma cells; regressive changes in the cells of the granular series; and not infrequently a polychromatophilic erythroblastic reaction, the degree of which is proportional to that of anaemia. Attention is drawn to the important bearing of myelotoxicosis on the origin of malarial leucopenia and anaemia. *C. M. Wenyon.*

TRIMARCHI, E. Comportamento dell'attività pessica del sistema reticolo-endoteliale in malarici sottoposti a cura adrenalinica venosa. [**The Fixing Capacity of the Reticulo-Endothelial System in Malaria Patients undergoing Intravenous Adrenaline Therapy.**] *Riv. di Malariologia.* 1946, Feb., v. 25, No. 1, 13–18. English summary (4 lines).

In his study of the fixing capacity of the reticulo-endothelial system the author employed the Congo Red Test (ADLER & REIMANN, 1925, *Ztschr. f. ges. exp. Med.*, v. 47, 617). Ten cc. of a 1 per cent. aqueous solution of Congo red are injected intravenously. Four minutes after the injection 4·5 cc. of blood are drawn into a syringe containing 0·5 cc. of a 5 per cent. solution of sodium citrate. A second withdrawal of blood is made in like manner 60 minutes after the injection. A colorimetric comparison of the citrated plasma, separated by centrifuge, is then made, the sample taken 4 minutes after the injection being used as the standard (four minutes is sufficient time for the dye to diffuse throughout the blood stream).

Twelve afebrile chronic malaria patients were examined, 10 infected with *P. vivax* and two with *P. falciparum.* The Congo Red test was made before, during and after treatment by Ascoli's method. The fixing capacity of the reticulo-endothelial system was markedly deficient in three cases and somewhat below physiological limits in others. The adrenaline treatment resulted in a prompt return to normality. *Norman White.*

BOWDEN, K. M., **Spontaneous Rupture of the Spleen, with Notes on Two Cases.** *Med. J. Australia.* 1946, Apr. 13, v. 1, No. 15, 506–8.

Notes are given of two fatal cases of spontaneous rupture of enlarged malarial spleens. Both patients were discharged service men, and both were aged 27. In both patients the spleen was greatly enlarged, 65 oz. in one case, 45 oz. in the second, dark in colour and extremely soft. Malaria had not been diagnosed in one of the cases during life. Many schizonts and ring forms of *P. vivax* were found in sections of the spleens. *Norman White.*

BILLI, A. Sulle rotture spontanee di milza malarica. [**Spontaneous Rupture of a Malarial Spleen.**] *Minerva Chirurg.* 1946, Sept., v. 1, No. 7, 209–12, 1 fig.

STEVENS, A. L. B. & BLACKMAN, G. G. B. **Benign Tertian Malaria in England.** [Correspondence.] *Brit. Med. J.* 1946, Oct. 26, 625.

This letter reports two cases of benign tertian malaria in persons who had never been abroad, and who, it is believed, contracted the infection in Oxford. Both patients lived within 60 yards of each other, near a slow-flowing branch of the Thames.

The first patient, a girl of 17, suffered from intermittent daily pyrexia for over a month, when trophozoites of *P. vivax* were found in her blood. She showed definite cycles of chills and shivering followed by heat and sweating. Other fevers were excluded by routine tests. Her symptoms were rapidly relieved by quinine. Her brother had been treated for a proved relapse of benign tertian malaria, acquired in Burma, whilst on leave in Britain in April 1946, after which he returned to his unit. After demobilization, he had lived at home since June 3rd, but had no further symptoms.

The second patient, a man of 47, had only left Oxford once in the last nine years. He suffered from fever nightly for about a fortnight, when a positive blood film was obtained. Antimalarial treatment relieved his symptoms. At the time of onset, he was convalescent from an attack of pneumonia which had begun about 19 days before the present febrile attack.

[This record should serve as a further warning to practitioners in Britain to bear in mind the possible need for examining blood films for malaria parasites in the case of all persons suffering from fevers of uncertain origin, irrespective of whether the patients had been abroad or not.]

H. J. O'D. Burke-Gaffney.

SHUTE, P. G. **Latency and Long-Term Relapses in Benign Tertian Malaria.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Oct., v. 40, No. 2, 189–200.

The author uses the phrase " a latent attack of malaria " to denote an attack of fever, with parasites, in a patient who had been infected several months before the development of clinical symptoms. Latent attacks of *P. vivax* malaria may occur under natural conditions, or as a result of drug prophylaxis, or in the presence of mixed concurrent infections (*P. falciparum* malaria developing in about 10 days, *P. vivax* malaria many months later), or when patients retaining an immunity to one strain of *P. vivax* are infected with another strain.

Interesting evidence is produced indicating that the number of sporozoites injected, in part at least, determines latency. It does not occur when the number is large; true latency only occurs when the number of sporozoites is too few to cause an immediate attack. The prolonged incubation period varies between 2 months and a year, frequently about 38 weeks. First relapses frequently occur after a similar interval.

It is suggested that relapses in *P. vivax* malaria are due to a resting phase of the parasite and that a drug which could prevent relapse would be a successful causal prophylactic. The author has shown that sporozoites may survive for many months in the tissue cells of the insect host and suggests that they may be able to do so in the human host.

Norman White.

HILLS, A. G. **Malarial Jaundice.** *Amer. J. Med. Sci.* 1946, July, v. 212, No. 1, 45–53. [13 refs.]

Of 8,837 patients suffering from malaria treated in a United States General Hospital in Assam only 24 (0·27 per cent.) had " malarial jaundice ". All were soldiers of the American or Chinese Army. Five of the 24 were *P. vivax* infections, the remainder *P. falciparum*. Jaundice did not occur in 100 cases of *P. malariae* infection. The three fatal cases were *P. falciparum* cerebral

infections. The average day of onset of the jaundice was the 4th day of fever (varying from the 1st to the 7th day); its average duration was 7 days (2 to 15 days). The average maximum van den Bergh reading in 10 patients was 2·4 mg. per 100 cc. In the other 14 patients, the average maximum icteric index was 27. In 6 patients, haemoglobin determinations showed that definite blood destruction accompanied the rising serum bilirubin, that is to say the jaundice was definitely haemolytic. Three patients passed free haemoglobin in the urine; two of them developed acute azotaemia (B.U.N. determinations 105 and 113). There was no indication that either quinine or atabrine played any part in the production of jaundice.

The conclusion is reached that haemoglobinuria will appear in malaria jaundice when the usual haemolytic mechanism present in the disease becomes so intense and acute that the reticulo-endothelial system is unable to keep the plasma haemoglobin level below the renal threshold.

The relationship of malarial jaundice to blackwater fever is discussed.

Norman White.

SHRAGER, J. & KEAN, B. H. **Purpura as a Complication of Malaria.** *Amer. J. Med. Sci.* 1946, July, v. 212, No. 1, 54–9. [17 refs.]

Among 10,000 consecutive cases of malaria treated in the Gorgas Hospital, Panama, there were only ten complicated by purpura. One patient who had received no antimalarial drug was admitted with purpura and made an excellent recovery after treatment with quinine. The other nine patients only developed purpura after the administration of quinine—9 patients out of 7,500 so treated. There was no purpura among more than 2,500 malaria patients treated with atabrine. Six of the 9 patients had *P. vivax* infections, 3 *P. falciparum*. Purpura affected the gastro-intestinal tract, genito-urinary tract, skin, conjunctiva, and respiratory tract in that order of frequency. The complication was a serious one; two patients died, one with a *falciparum* the other with a *vivax* infection. All ten patients were white American adults; no native patient, of whom there were many, developed purpura. The case histories of patients suggest that the purpura due to quinine was not a simple toxic manifestation but was an allergic reaction.

Norman White.

KARK, W. **Surgery and the Relapse Rate of Malaria.** *Brit. Med. J.* 1946, July 27, 114–17.

Records published in this paper indicate that the risk of activating latent malaria attendant upon surgical operations has been somewhat over emphasized. One hundred and seventy-six operations were performed on 153 patients with a pre-operation history of malaria but who had received no suppressive malaria therapy, either before or after operation. In only 10 per cent. of these cases was there a post-operation attack of malaria fever. Some of these attacks may not have been relapses. The hospital was in an endemic area. The relapse rate was no greater after a major than after a minor operation; for this purpose a minor operation is one that was done in less than 20 minutes. The use of local anaesthetics containing adrenaline was followed by a higher proportion of attacks of fever than was the use of other forms of anaesthesia. Post-operation relapses were predominantly due to *P. vivax*.

A further series of 147 operations were performed on patients who had received and completed suppressive treatment before operation. The rate of post-operation attacks of malaria in this group was not significantly different from that in the first.

One thousand nine hundred surgical cases were seen in a forward hospital. The battles had taken place in hyperendemic country. All these patients had

been taking suppressive mepacrine, 0·1 gm. daily, and this was continued during the evacuation stages and during the stay in hospital. Only two cases of post-operation malaria were seen, and in both cases there was reason to believe that the patients had evaded taking the daily dose of mepacrine.

Norman White.

LISITSA, F. M. [**Neurological Symptoms of Comatose Malaria.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1946, v. 15, No. 1, 44–50. [In Russian.]

The author emphasizes the importance of a differential diagnosis of the nervous symptoms in malignant tertian malaria, and discusses the symptomatology of comatose malaria on the basis of literary data and personal observations. It is pointed out that in endemic areas of malaria, care should be exercised in distinguishing malarial coma from similar conditions of non-malarial origin, though in suspicious cases, where there is some doubt, anti-malarial treatment should not be delayed. Although disturbances of consciousness represent the most characteristic symptom of comatose malaria, they cannot alone serve for early diagnosis and prognosis. In characteristic cases of coma there are other peculiar changes in the neurological signs, *viz.* disturbances of muscular tone, tonic labyrinthine ocular reflexes and other disturbances of tonus, local and generalized convulsions, changes in the reflexes and disturbances of the autonomic nervous system. Though treatment of comatose malaria is not dealt with specifically, the author recommends transfusion of blood plasma as a useful supplementary measure. In cases with a tendency for convulsions, injection of camphor is contraindicated.

C. A. Hoare.

DELL, J. M., Jr. & KLINEFELTER, H. F., Jr. **Roentgen Studies of the Spleen.** *Amer. J. Med. Sci.* 1946, Apr., v. 211, No. 4, 437–42, 6 figs.

The studies reported were carried out with the object of finding an objective and accurate method for determining the size of the spleen. Some enlarged spleens are not palpable and some palpable spleens are not enlarged.

In a U.S. Army General Hospital, the spleens of 300 patients were X-rayed. Half of these had either palpable spleens or were suffering from diseases which might cause splenic enlargement. Postero-anterior films were taken before meals. The plates were made in the PA projection, with a Potter-Bucky diaphragm, 100 milliamperes, with a time exposure of 0·5 second, at a target film distance of 36 inches. The kilovoltage, varying with the thickness of the patient, averaged 6 to 8 kv. less than the usual stomach technique. The central ray was directed halfway between the midline and the left lateral chest wall, three finger breadths below the ensiform cartilage.

There is a considerable variation in the size of normal spleens in different persons ; in general, the size of the spleen varies with the size of the subject. Any rotation of the spleen will decrease its apparent size, but there is a corresponding increase in density. Density was measured by comparing it with that of the lower half of the left kidney ; the density was considered increased if it was greater than that of the normal kidney. A spleen was considered enlarged if it was more than 6 cm. in width or more than 85 per cent. the size of the kidney. In most cases the size of the spleen could be definitely and readily determined from the roentgenogram. No diurnal variation in the size of the spleen was noted and no variation in relation to food or moderate activity. There was often a definite decrease in spleen size, 5 to 15 minutes after subcutaneous injection of adrenalin.

Norman White.

VOGT, E. Et tilfelle av malaria i Oslo. [**A Case of Malaria in Oslo.**] *Nordisk Med.* 1946, Nov. 8, v. 32, No. 45, 2601–2. [Summary in English by the author.]

"A case of malaria tertiana in a woman of 55 years, townbred and living in Oslo, is reported. This woman had never been abroad and there were no clues for incubation with malaria. The first clinical symptoms of the disease were noticed in March 1946, at a time when the anopheles of this country are hibernating. She was therefore believed to have caught the infection in the course of the preceding summer (July–August 1945) when spending her vacation in a neighbourhood where anopheles have been found, and where at the time there were carriers of the disease (military troops from malaria districts). The incubation period for this case is thus calculated at 8–9 months. Attention is directed to the fact that an equally long incubation time for malaria has often been observed also in the Netherlands and in Great Britain."

TEASLEY, G. H. **Malaria following Blood Transfusion : Report of Case.** *Proc. Staff Meetings Mayo Clinic.* 1946, Aug. 7, v. 21, No. 16, 289–93. [20 refs.]

"This report is based on a case in which malaria was transmitted by blood transfusion. It should always be borne in mind that suppressive atabrine therapy gives no guarantee that the patient will not become a carrier of malarial parasites. The appearance of undetermined fever or chills and fever approximately a week after transfusion of blood should lead to a suspicion of the transmission of malaria. Thick blood smears should be made and examined immediately by a competent person. The endemic malarial areas of the world should be known by every physician, and blood donors from these areas should not be accepted without thorough investigation. Blood obtained from a suspicious person should be stored for a minimum of eight days before use. At present, there is no laboratory test that definitely will exclude all malarial carriers as prospective donors."

MERKEL, W. C. *Plasmodium falciparum* **Malaria. The Coronary and Myocardial Lesions observed at Autopsy in Two Cases of Acute Fulminating** *P. falciparum* **Infection.** *Arch. Pathology.* 1946, Mar., v. 41, No. 3, 290–98, 6 figs.

An account is given of two patients with *P. falciparum* infections which ran an extremely rapid course. Death in both cases was typical of cardiac dilatation and collapse ; neither was in actual coma. The description of the post-mortem findings is illustrated by excellent photomicrographs. Parasites and parasitized red cells are seen adhering to the capillary walls in the myocardium ; only amoeboid forms are lined along the inner surface of the vessels. The endothelial cells of the capillaries are swollen and often contain phagocytosed malarial pigment. The lesions in the heart resemble infarcts. During the time that these occlusions exist the heart must experience anoxaemia proportional to the extent of the area involved. The coronary system of the heart has a poor collateral circulation, and it would seem that coronary occlusions producing anoxaemia of the heart may be as important a factor in fatal cases of *P. falciparum* malaria as the occlusion of cerebral vessels. *Norman White.*

MAYER, M. M. & HEIDELBERGER, M. **Studies in Human Malaria. V. Complement-Fixation Reactions.** *J. Immunology.* 1946, Sept., v. 54, No. 1, 89–102, 1 fig. [17 refs.]

The antigens most frequently used in this study were the crude *Pl. falciparum*, the crude *Pl. vivax* and the more highly purified *vivax* antigen (soluble *vivax*

antigen), all prepared from citrated human blood by methods previously described. In addition a normal human stromata antigen was used. The sera were absorbed with sheep cells and tested at a dilution of 1:10 with four 50 per cent. units of complement. Primary fixation was for 40 minutes at 37°C. In the case of Wassermann positive sera, it was necessary first to absorb the sera with Kahn floccules, since the malarial antigens contained the Wassermann antigen. This antigen was predominantly contained in the plasmodium and only to a limited extent in normal erythrocytic stromata. The specific malarial antibody was distinct from the accompanying Wassermann antibody.

With sera from cases of chronic relapsing *vivax* malaria, fixation was most often observed with the soluble *vivax* antigen, the crude *vivax* antigen being somewhat less reactive. In the majority of the sera which gave good fixation with the crude *vivax* antigen, equally good fixation was obtained with the normal human stromata antigen. The antibody which reacted with the normal stromata was distinct from the specific malarial antibody, but attempts to differentiate them clearly by absorption were equivocal because intact human red blood corpuscles failed to absorb the antibody and absorption with the stromata antigen rendered the sera anticomplementary. This auto-antibody was quite distinct from the Wassermann antibody. With the soluble *vivax* antigens, the antibody to the plasmodial component was being measured, whereas with the crude *vivax* antigens the auto-antibody was mainly being titrated. However, the latter reaction, although immunologically non-specific, was characteristic for malaria as a disease. The sera from these cases of chronic relapsing *vivax* malaria were also combined with other antigens prepared in similar ways of *Pl. gallinaceum*, *Pl. knowlesi* and of normal chicken and monkey stromata. The monkey stromata antigens were all negative but the other antigens gave fixation similar to the normal human stromata antigens, presumably reacting with the auto-antibody.

The crude *falciparum* antigen reacted with these same sera less strongly than the normal human stromata antigens, because the former was used at a higher dilution. However, with sera from cases of *Pl. falciparum* infection, the *falciparum* antigens reacted strongly where there was no fixation with soluble *vivax* antigens. Fixation was only obtained with the crude *vivax* antigens in those cases which because of their auto-antibody also fixed complement with normal human stromata antigens. This indication of a species specificity in the immune response was also noticed with sera from patients infected with either *Pl. falciparum* or *Pl. vivax*, and also with sera from patients who had received formalinized vaccines of these plasmodia.

The authors conclude that as a test for latent malaria the complement fixation reaction with any of the antigens described is of only limited value. If syphilis is excluded a positive reaction either with a malarial antigen or with a preparation of normal human stromata is specific for malaria. But with sera from cases of chronic relapsing *vivax* malaria, a single examination with the most reactive antigen (soluble *vivax* antigen) only gave fixation in 40 per cent. of cases. However, by repeatedly testing such patients over 2–3 months the probability of detecting malaria is much greater.

The specific malarial antibody did not appear to be a protective antibody. The auto-antibody possibly indicated a lack of immunity. *Forrest Fulton.*

Gordon, H. H., Marble, A., Lippincott, S. W., Hesselbrock, W. B. & Ellerbrook, L. D. **Clinical and Laboratory Studies of Relapsing Vivax Malaria of Pacific Origin.** *New England J. of Med.* 1946, Apr. 18, v. 234, No. 16, 519–23, 1 fig. [11 refs.]

This is a study of the clinical features and laboratory findings in 808 soldiers admitted to the Malaria Section of the Harmon General Hospital. All the

patients had acquired *P. vivax* infections in the Pacific war areas. *P. falciparum* was only once found, in a mixed infection, an indication of the efficacy of mepacrine in curing malignant tertian malaria.

Gametocytes were found in 49 per cent. of smears taken during 401 attacks, but even when treatment was delayed 48 hours after the onset of the attack, two or more gametocytes per 100 white cells were found in only 16 per cent. of attacks. Prompt treatment quickly eradicates parasites, so that if the disease is recognized promptly and treatment started without delay, there is very litle danger of its transmission by gametocytes. No locally-acquired malaria has occurred at this hospital during the eighteen months during which malaria has been treated there.

Acute attacks were relatively mild, but the tendency to relapse was very marked. Attacks were treated with quinacrine (mepacrine), 0·2 gm. every six hours for 5 doses, then 0·1 gm. thrice daily for 6 days. Symptoms of the acute attack were quickly controlled by doses of mepacrine that gave a fasting plasma concentration of 40 to 50 microgm. per litre. Between attacks, many patients complained that they were easily fatigued, and of nervousness and dyspepsia. Sixty-seven per cent. of the patients relapsed within 60 days after the completion of treatment. The administration of small doses of mepacrine or of pamaquin had no significant effect on the ultimate rate of relapse, though very few relapses occurred when patients were actually taking 0·1 gm. mepacrine a day (only 4 relapses in 163 patients).

The complement-fixation test with a *P. gallinaceum* antigen was not of much value in detecting latent malaria between attacks. Sixty-four per cent. of 891 tests so performed were negative.

Liver function tests showed no evidence of permanent hepatic dysfunction.

Norman White.

CARLSON, H. J., MUELLER, M. G. & BISSELL, H. D. **Colorimetric Diagnostic Tests for Malaria.** *J. Lab. & Clin. Med.* 1946, June, v. 31, No. 6, 677–86, 3 figs. [12 refs.]

The work described was done with the aim of finding an aid to the diagnosis of malaria in cases in which parasites are not demonstrable in the peripheral blood. The considerations that melanin in colloidal solutions has properties similar to those of solutions of certain colloidal dyes and that colloidal dyes, under certain conditions, combine quantitatively with proteins, suggest that the use of such dyes might demonstrate the modified characteristics of malaria serum during the acute and chronic phases of the disease. The test evolved is done as follows :—

One cc. of a 0·1 per cent. aqueous solution of Congo red is placed in a test tube (13 by 100 mm.) and 0·5 cc. of the non-inactivated serum to be tested is added. The mixture is well shaken. Two cc. of a 0·3 per cent. aqueous solution of quinine hydrochloride are then added ; complete mixing is obtained by inversion of the tube. The tube remains at room temperature for 45 minutes, and is then centrifuged for 10 minutes, 3,500 to 4,000 r.p.m. One cc. of the clear supernatant fluid is transferred to a graduated cylinder and diluted to 60 cc. with distilled water. One drop of N/10 NaOH is added to the diluted mixture. A 19 by 105 mm. cuvette is filled with distilled water as a reference standard and the galvanometer needle of a spectrophotometer is set to zero optical density with water in the cuvette well, using a wave length of 500 mm. the point of maximum adsorption by the red-orange solution. The optical density of each test solution is read in turn and the values are recorded as directly proportional to the dye left in solution.

Observations were made on monkeys with *P. knowlesi* infections, on bird malaria (*P. gallinaceum*) and on human *P. vivax* malaria. By way of illustration

of results the following is given :—Optical densities in monkey O before infection varied from 0·400 to 0·460, over a ten-day period. Three days after infection the reading was 0·420 ; thereafter readings fell steadily to 0·190 on the 16th day of infection. After treatment with atebrin the readings gradually returned to normal

It is possible that this reaction has no specific relationship to a malaria infection, but controls, other than serum from patients with infectious hepatitis or marked anaemia, showed no similar reactions. It, or a modification of it, might be a significant diagnostic aid in malaria. *Norman White.*

FISCHER, H. & ALMASY, F. I. Ueber die Wirkung des Chinins auf Mikroorganismen. Ein Beitrag zur Grundlegung cellulärer Wirkungen pharmakologisch aktiver Stoffe. [**The Action of Quinine on Micro-Organisms. The Cellular Effect of the Active Principle.**] *Arch. f. Exper. Path. u. Pharm.* 1942/43, v. 200, 455–94, 15 figs. [39 refs.]

FAIRLEY, N. H. **The Chemotherapeutic Control of Malaria.** *Schweiz. med. Woch.* 1946, v. 76, Nos. 37/38, 925–32. [13 refs.]

The important investigations described here were carried out by the Australian Medical Research Unit at Cairns, Australia, during the late war and were the subject-matter of a lecture given to the British-Swiss Medical Conference at Basle, in September 1946. The author briefly discusses the two different problems of chemotherapeutic control of malaria in non-immune populations as represented by troops in the field and in indigenous populations already possessing some immunity. Observations on this subject by SINTON have been reviewed [this *Bulletin*, 1940, v. 37, 57] and at different times those of other writers. During 1942 and 1943 in the S.W. Pacific area, where malaria was a serious problem amongst troops engaged in jungle warfare, quinine had at the start been chiefly employed as a suppressant but proved unsatisfactory. A Research Unit was therefore set up at Cairns and investigated the suppressive and causal prophylactic action of various drugs. About 850 healthy volunteers were infected with sporozoites during these experiments. The drugs tested were : quinine, plasmoquine, atebrin, certain sulphonamides, paludrine (M4888) and its methyl derivative (M4430) as well as two drugs of the 4-aminoquinoline series, sontochin (SN 6911) and resochin or chloroquine (SN 7618) which were first synthesized in Germany and supplied from America. Some earlier reports on treatment with M4888 and M4430 have been reviewed [this *Bulletin*, 1946, v. 43, 400–402, 527, 628]. Of the above series quinine, atebrin, sulphadiazine, sontochin and resochin had suppressive properties through their action on schizonts. However, by the technique of subinoculating non-immunes with 200 cc. whole blood of a treated donor on the 7th and 9th days respectively after infection with *P. falciparum* and *P. vivax* the presence of viable parasites in the donors' blood was demonstrated. While quinine and sulphonamides proved of little value as suppressants for Army purposes, it was found that with the atebrin, sontochin and resochin then available malaria due to *P. vivax* could be suppressed while the drug was being taken and brought about radical cure of *P. falciparum* infections through schizonticidal action as distinct from that on pre-erythrocytic forms. The above technique of subinoculating whole blood allowed drugs to be classified as schizonticidal suppressants or causal prophylactics. In the latter category was plasmoquine, which in doses too large to be tolerated proved to be a complete causal prophylactic in malignant tertian malaria and a partial causal prophylactic in benign tertian malaria, as previously reported by JAMES and collaborators in 1935 as a result of their experiments at Devon Mental Hospital. Paludrine in well-tolerated doses had similar properties, was very active in

the cure of clinical attacks and appeared to be the most effective drug in the radical cure of malignant tertian malaria in the S.W. Pacific area. In the case of B.T. malaria the clinical response to treatment with this drug was not superior to that obtained with quinine or atebrin. Plasmoquine-paludrine therapy was, however, more effective than quinine-plasmoquine treatment in lengthening the period between relapses. A striking property of paludrine was its ability in the small single dose of 100 mgm. to cause disappearance of parasites and symptoms in BT and MT infections and in the author's words: "The possibilities of this single dose regimen of paludrine applied to native villages and epidemics in hyperendemic areas open up an entirely new field in the chemotherapeutic control of this disease, not only on account of its schizonticidal value, but also because of its extraordinary potency as a causal prophylactic." The result of extended field experiments will be eagerly awaited.

J. D. Fulton.

BLACK, R. H. **The Effect of Anti-Malarial Drugs on** *Plasmodium falciparum* **(New Guinea Strains) developing** *in vitro*. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1946, Oct., v. 40, No. 2, 163–70, 6 coloured figs. on 1 pl. [10 refs.]

In spite of much experimental work no definite evidence has been obtained regarding the mode of action of drugs on malarial parasites. In the present investigations, the qualitative action of a number of compounds of widely different chemical constitution has been studied on various New Guinea strains of *P. falciparum in vitro*. Infected blood was obtained from volunteers of blood group O who were experiencing a primary attack. By this means agglutination or lysis of red cells of other groups was avoided and the amount of immune bodies in the serum used was minimal. The method of cultivation was that described by the author [this *Bulletin*, 1946, v. 43, 816] in which a large excess of serum admixed with glucose was incubated with a small volume of infected cells, and development of a proportion of the parasites was observed through at least one generation. In observing the effect of a drug on the parasites, serum from a donor treated orally or intramuscularly with the drug in question was used in the culture tubes, and in the case of quinine, atebrin, and sulphonamides the amount of drug present was estimated. Samples were withdrawn from the cultures at intervals of 4 to 6 hours for morphological studies. In the control tubes, serum from the donor of infected blood as well as from healthy donors was used. The lethal effect of paludrine (M4888), and of the closely related M4430, was exerted on young schizonts in a similar way to that noted in treated cases of *P. vivax* malaria. Atebrin, sontochin (SN6911) resochin or chloroquine (SN7618) and quinine caused arrest of development and degeneration of parasites at an earlier stage. In the presence of sulphonamides parasites developed normally up to the time of segmentation of chromatin. With plasmoquine, constant results were not obtained. The infected red cell thus appears to be permeable to drugs before the segmenting stage of the parasite is reached. Provided the mature schizont stage of the parasite was reached in presence of any particular concentration of a drug, the invasion of new red cells by merozoites appeared to be unhindered.

J. D. Fulton.

GORDON, H. H., CHRISTIANSON, H. B. & LIPPINCOTT, S. W. **A Comparison of Quinine and Quinacrine in the Treatment of the Clinical Attacks of Vivax Malaria.** *Southern Med. J.* 1946, Aug., v. 39, No. 8, 631–4, 1 fig.

Quinacrine was used in the treatment of 253 cases of relapsed *vivax* malaria, and quinine in the treatment of 55. Infection in all cases had been contracted in either the Pacific or the Mediterranean war areas. The dosage of quinacrine was 1·0 gm. during the first 24 hours and then from 1·6 to 2·2 gm. given during the

subsequent 5 or 6 days. Quinine sulphate dosage was 1·0 gm. thrice daily for 2 days followed by 0·64 gm. thrice daily for 5 days. No patient was treated unless his oral temperature exceeded 100°F. and unless parasites were found in the blood. The patients were well nursed and fluids were forced in all cases. Quinacrine cleared the blood of parasites much quicker than did quinine. Both drugs satisfactorily controlled fever. Minor toxic symptoms were much more in evidence with quinine. Quinacrine is the drug of choice in the treatment of *vivax* relapses and not a mere substitute for quinine. *Norman White.*

READ, H. S., BECKER,, F. T. & KAPLAN, L. I. **Operation of an Army Neurosyphilis Center.** *Bull. U.S. Army Med. Dept.* 1946, July, v. 6, No. 1, 66–71.

This is a brief description of the administration and working of a Neurosyphilis Centre at a U.S. Army General Hospital. During a period of 17 months 636 patients were admitted of whom 373 received malaria therapy. The single fatality in this series of cases was caused by spontaneous rupture of the spleen. *Norman White.*

BECKER, E. R., BURKS, C. S. & KALEITA, E. **Plasma Atabrine Concentrations attained by Subjects taking 0·1 Gram of the Drug Daily.** *J. National Malaria Soc.* Tallahassee, Fla. 1946, June, v. 5, No. 2, 165–8.

"The mean plasma atabrine levels of a group of 14 individuals under observation for 21 weeks commencing 15 February '45 in Assam, India, stabilized within two weeks on a suppressive atabrine regime of 0·1 gm. daily at values ranging from 21·3 G/L to 26·0 G/L. A group of seven others who started at the same time attained somewhat lower means, apparently because this group contained four individuals who might be called 'poor absorbers'. There was considerable variation in the ability of individuals to attain blood levels recognized as satisfactory for suppression. These groups contained no individuals who exhibited extraordinarily high blood levels, but a number of such cases were encountered in the course of other studies and are herewith described."

SMITH, P. K., GALLUP, Barbara N. & CAIN, Louise J. **Blood Plasma Atabrine Levels obtained with Suppressive and Therapeutic Doses of Atabrine Dihydrochloride.** *J. Pharm. & Exper. Therap.* 1946, Aug., v. 87, No. 4, 360–63, 2 figs.

"1. The blood plasma levels of subjects receiving the same dose of atabrine are extremely variable.

"2. The group average plasma levels obtained are approximately proportional to the dose used.

"3. With constant daily doses four to five weeks are required to reach constant mean plasma levels. Similar plasma levels are reached in two weeks when the dose is doubled during the first week.

"4. With low plasma levels of atabrine a reduction to one-half occurs in approximately two weeks after administration of the drug ceases. With a large dose and high plasma levels the reduction is more rapid.

"5. Moderate doses of sodium bicarbonate or of ethyl alcohol do not affect the plasma levels."

LUTTERLOH, C. H. & SHALLENBERGER, P. L. **Unusual Pigmentation developing after Prolonged Suppressive Therapy with Quinacrine Hydrochloride.** *Arch. Dermat. & Syph.* 1946, Apr., v. 53, No. 4, 349–54, 7 coloured figs. on 1 pl.

The authors have seen eight cases of unusual pigmentation that have followed prolonged administration of mepacrine. Detailed reports of three cases are

given. There was blue-grey pigmentation of the nails of fingers and toes. The pigmentation was situated in the nail-bed ; diffuse in most cases but sometimes as a transverse band near the middle of the nail. In one case there was light-bluish pigmentation of the tip of the nose and inferior surfaces of the alae, and a dark-bluish discoloration of the hard palate. Abstention from mepacrine for four months in one case resulted in marked improvement ; the abnormal pigmentation had cleared considerably.

The blue-grey colour is in striking contrast to the lemon hue of mepacrine staining of the skin. A possible explanation is that the optical scattering phenomenon exhibited by the skin may cause pigment deposited in the corium to assume a grey to blue colour, depending on the amount and depth of the pigment. [See also this *Bulletin*, 1946, v. 43, 1008.] *Norman White.*

D'IGNAZIO, C. & COLLOMB, H. Neuro-psychoses aigües consécutives à l'administration d'atébrine. [**Acute Neuro-Psychoses following the Administration of Atebrin.**] *Boll. Soc. Ital. di Med. e Igiene Trop.* (Sez. Eritrea). 1946, v. 6, Nos. 1/2, 43–51.

An account of two cases.

JAME, L. Quelques aspects de la prophylaxie du paludisme en Afrique du Nord au cours de la guerre mondiale. [**Certain Aspects of Malaria Prophylaxis in North Africa during the World War.**] *Bull. Soc. Path. Exot.* 1946, v. 39, Nos. 1/2, 17–28.

During the early years of the world war when the three countries of North Africa were more or less cut off from France there was a growing shortage of antimalarial drugs and of larvicidal substances. The native population suffered accordingly. In Algeria the spleen rate which before 1940 varied between 33 and 38 reached 55 after the epidemic of 1943. Undernourishment was also an important factor in the deterioration of health conditions. Later the reservoir of infection was reinforced by the arrival of large numbers of prisoners of war, many of whom, notably Italians, were heavily infected. Then the arrival of large numbers of non-immunes, American and British troops and Frenchmen from France travelling across Spain, increased the danger of an epidemic. Prophylactic measures, however, were successful in large measure in protecting the military forces. Statistical information regarding the incidence of malaria in the civil population is incomplete. Among troops in Morocco, malaria increased year by year from 1939 to 1943 ; there were 6,233 cases in 1943 as compared with 1,354 in 1939. In 1944 there was an abrupt decline. Rainfall was deficient in 1944 and antimalarial measures of many kinds were renewed with materials obtained from American sources. There was a parallel improvement in the civil population. Similar trends in malaria incidence were noted in other parts of North Africa.

The paper includes a dissertation on the value of synthetic drugs in the clinical prophylaxis of malaria. *Norman White.*

GUNTHER, C. E. M. **New Conceptions of Malaria Control.** *Med. J. Australia.* 1946, Apr. 13, v. 1, No. 15, 510–11.

The author considers malaria control in the light of results achieved with new drugs and new insecticides. Atebrin is passing out of the picture : without strict military discipline atebrin would have failed in the war ; such discipline is impossible in peacetime. Moreover the risk of toxic effects of atebrin are not justifiable in civilian practice. Paludrine will take its place ; it is a true causal prophylactic of *P. falciparum* malaria and a complete suppressant of

benign tertian fever in a dose of 0·1 gm. twice a week. "A single dose of 0·1 gramme ends an attack of either benign or malignant tertian fever and brings the temperature to normal. This is the end of hospitalization, of malaria cachexia, of malarial abortions, of heavy infantile mortality due to cerebral malaria, of enlarged, easily ruptured spleens and of blackwater fever." All susceptible comers to malarious districts should take 0·1 gm. of paludrine twice a week, but it is preferable that indigenous natives should not have their acquired tolerance interfered with in this way. For them a single dose should be given to control occasional attacks of malaria fever.

Consideration is also given to the extreme value of DDT and "666" in mosquito control, and of di-methyl phthalate as a mosquito repellent.

Norman White.

VAUCEL, M. État actuel du paludisme dans les colonies françaises. [**Existing Conditions with regard to Malaria in French Colonies.**] *Bull. Soc. Path. Exot.* 1946, v. 39, Nos. 1/2, 29–36.

This paper describes the dominating position that malaria occupies in the nosography of the French colonies and the inadequate measures that, with few exceptions, are taken to diminish its prevalence. It appeals, for the understanding and support of Administrations in a widespread application of modern methods of malaria prophylaxis and control. *Norman White.*

MASILLAMANI, S. G. **A Paris Green Distributor.** *J. Malaria Inst. of India.* 1946, June, v. 6, No. 3, 263–4, 1 fig. & 1 pl.

NÁJERA ANGULO, L. Consideraciones sobre la "Gambusia Holbrookii" y método para conseguir la repoblación autobiológica de los ríos. [**Considerations concerning** *Gambusia holbrooki* **and a Method of conserving the** *Gambusia* **Population in Rivers.**] Reprinted from *Rev. Ibérica de Parasit.* Granada. 1945, Oct., v. 5, No. 4, 331–42, 3 figs.

This is a dissertation on the value of *Gambusia holbrooki* as a larvicide in malaria control, the extent of its use in Spain for that purpose, and its adaptability to a large range of temperature and of water salinity. A plea is made for its more extended use in Spain. A description is given of a tank, adjacent to the bank of a river, in which *Gambusia* thrive and breed abundantly.,

Norman White.

NÁJERA ANGULO, L. A luta anti-larvar: agentes biológicos e recursos similinaturais. [**Biological and Naturalistic Antilarval Measures.**] *An. Inst. Med. Trop.* Lisbon. 1945, Dec., v. 2, 275–327, 44 figs. (29 on 15 pls.).

This lecture is a comprehensive survey of certain measures of mosquito larval control including drainage, automatic flushing, fascine drainage and the use of *Gambusia.* On the last subject the author's remarks are an amplification of his paper published in the *Revista Iberica de Parasitologia* (see above).

Norman White.

MASILLAMANI, S. G. **A Net for catching** *Gambusia* **Fish from Nurseries, Tanks and Wells.** *J. Malaria Inst. of India.* 1946, June, v. 6, No. 3, 259–61, 1 fig.

WILSON, D. Bagster. **Notes on the Use of Spray Killing against Mosquitoes.** *East African Med. J.* 1946, May, v. 23, No. 5, 131–9. [14 refs.]

Experience in the spray-killing of adult mosquitos while serving with the army in East Africa has led to conclusions which are set out in this paper. In

unclosed, or partially closed, buildings the "direct hit" is essential and for this the average flitgun, as ordinarily used, is an ineffective weapon; hand atomizers urgently need improvement. Against tropical African vectors, *A. gambiae* and *A. funestus*, spraying is required daily, in the evening. Pyrethrum is at present an essential constituent of an effective spray but some DDT should be added. Military experience gives no grounds for supposing that spray-killing alone can do more than effect a very partial reduction in malaria transmission in hyperendemic areas of tropical Africa.

Norman White.

RIBBANDS, C. R. **Repellency of Pyrethrum and Lethane Sprays to Mosquitos.** *Bull. Entom. Res.* 1946, Sept., v. 37, Pt. 2, 163–72.

An account is given of investigations into the repellent effect of certain insecticides used for killing house-haunting mosquitoes.

The experiments were conducted in coolie huts in Assam between July and October 1945. Most of the huts had mud walls and thatched roofs; they were open at the eaves and there were no windows. Each hut contained two rooms each about 10 feet by 10 feet. The mosquitoes were a mixed population of anophelines and culicines; 75 per cent. of the anophelines were *Anopheles minimus* and the rest were mainly *A. varuna* and *A. fluviatilis*.

The spraying and catching technique was standardized throughout. Doses of the insecticides averaged 50 cc. of 0·1 per cent. pyrethrum in kerosene (=0·05 cc. pyrethrins), or fifty seconds of aerosol spraying (=0·075 cc. pyrethrins), or 25 cc. of 10 per cent. Lethane 384 in kerosene.

Tabulated results show the extent of repellency by expressing the catch after different intervals as a percentage of the same catch after a five-day interval when the repellent effect was assumed to be negligible. These results show that the extent and persistence of the repellent effect varied with the insecticide, time of spraying and the intervals between treatments; also that sensitivity to the repellent effect varied with the species and sex of the mosquito.

For example, spraying with 0·1 per cent. pyrethrum led to a reduction of infestation by fed *A. minimus* by 90 per cent. after the first night, 60 per cent. after the second night and the repellency persisted in diminished degree for at least four days. *A. minimus* was more sensitive than *A. vagus* and males were more sensitive than females. The pyrethrum aerosol produced similar though less marked effects and males were again more sensitive than females. In similar experiments with Lethane, though there was some evidence of repellent effect it had worn off by the second night. In other experiments with Lethane, which involved repeated catches, opposite results were noted; female *A. minimus* were more sensitive than males and male *A. vagus* were more sensitive than male *A. minimus*.

As an insecticide Lethane gave a quicker knockdown than pyrethrum but where the repellent effect is of no consequence the latter is preferable as it is not so unpleasant as Lethane. The rate of knockdown is even slower with pyrethrum aerosol and the chance of escape is increased. "Discovery of an efficient insecticide possessing no residual repellent or masking effect would be a considerable contribution to modern technique." *H. S. Leeson.*

BRADLEY, G. H. & FRITZ, R. F. **Entomological Evaluation of DDT Residual Spraying for Malaria Control.** *J. National Malaria Soc.* Tallahassee, Fla. 1946, June, v. 5, No. 2, 141–5.

"1. Residual deposits of DDT were applied to some 400,000 homes for control of malaria during 1945.

"2. Such deposits were highly effective in keeping houses free of resting anopheline mosquitos.

"3. Effectiveness of DDT deposits, as measured by the percentage of sprayed houses found free of live mosquitos, gradually decreased during successive months following application. However, after 4 months, live mosquitos were found in only about eight per cent. of treated houses examined.

"4. There was an apparent reduction of 85 per cent. in the number of *quadrimaculatus* mosquitos which had human blood meals in sprayed areas as compared to unsprayed areas."

KNIPLING, E. F. **Recent Developments in the use of DDT and other Mosquito Insecticides and Repellents.** *J. National Malaria Soc.* Tallahassee, Fla. 1946, June, v. 5, No. 2, 113–21. [12 refs.]

CAMBOURNAC, F. J. C., SIMÕES, J. M. P. & QUEIROZ, E. J. S. Novo método de combate às larvas de *Anopheles*, nos arrozais, por meio de substâncias do grupo D.D.T. [**New Method of destroying Anopheline Larvae in Rice-Fields with DDT Preparations.**] *An. Inst. Med. Trop.* Lisbon. 1945, Dec., v. 2, 103–39. [12 refs.] English summary.

The investigations recorded in detail were carried out in a hyperendemic region where the only vector, *A. maculipennis* var. *atroparvus*, breeds extensively in ricefields. Good results were obtained with a 1 per cent. alcoholic solution of DDT, either alone or with the addition of "Molhante" NNE (Geigy) 0·25 cc., and turpentine 0·125 cc., to each 5 cc. The larvicide is mixed with the water at the spot where it enters the irrigated field. The extreme diffusibility of the alcoholic solution makes the distribution of the larvicide automatic. Plots as large as 100 metres long and 30 metres broad were easily treated in this manner. The stage of development of the rice crop is immaterial. Dilutions as high as one in ten to twenty million of the total water in the plot were very lethal to anopheline larvae, and toxicity was pronounced in dilutions up to one in a hundred million. *Norman White.*

STAGE, H. H. **Species Eradication by means of DDT.** *J. National Malaria Soc.* Tallahassee, Fla. 1946, June, v. 5, No. 2, 99–101.

BRITISH GUIANA. **Report of the Malaria Research Service Medical Department —British Guiana, for the Year 1945** [GIGLIOLI, G., Hon. Govt. Malariologist]. 76 mimeographed pp., 3 diagrams.

During 1945 the Malaria Research Service of British Guiana was mainly concerned with investigations on DDT. The only vector of malaria of any importance in the Colony is *A. darlingi*. This species has a maximum observed life span of 34 days. The females are voracious feeders; they take their first blood meals 24 hours after emerging and continue to feed every other night. They are strictly nocturnal in their habits and rarely attack in the open; they feed selectively on man and enter houses in large numbers, resting on walls, furniture and hangings before feeding, and, if undisturbed, remaining in the house for long periods after feeding; they are very susceptible to malaria infection, sporozoites developing in 11 or 12 days after the infecting meal. These habits make *A. darlingi* peculiarly vulnerable to DDT. Insecticide sprays with prolonged residual action, such as is characteristic of DDT, will affect also *Culex fatigans*, a carrier of filariasis which is a major problem, and *Aëdes aegypti* the vector of yellow fever, which is a potential danger. The early trials with DDT described in this report have given results of great promise. In villages on the

east coast of Demerara, mosquito captures in dwellings that had been sprayed with 5 per cent. DDT in kerosene were reduced by upwards of 98 per cent., as compared with unsprayed control houses, during the nine or ten months that followed the spraying. The reduction in the numbers of *A. darlingi* was greater than that of *C. fatigans*, but was remarkable in both. A significant fall in spleen and parasite rates followed the spraying.

A. darlingi has been shown to be a very highly efficient vector of filariasis.

These preliminary investigations on DDT are described in detail; an adequate summary is not possible. Further reports will be awaited with much interest. [See also SYMES and HADAWAY, this *Bulletin*, 1945, v. 42, 785.]

Norman White.

MACDONALD, G. **Notes on Malaria and its Control for Planters and Miners.** 1946, Apr., 61 pp., 11 figs. & frontispiece. Published under the Authority of the Ross Institute Industrial Advisory Committee by the Malayan Chamber of Mines (Incorporated) and the Rubber Growers Association (Incorporated). London School of Hygiene and Tropical Medicine (University of London) incorporating the Ross Institute.]

The foreword of this useful booklet states " The object of the notes is to give moderately full information on the method of dissemination of malaria and of the technique of its control in such a form that the planter or miner can institute control himself if he is unable to get specialized advice on how to set about it." That object has been accomplished with noteworthy success. All essential facts have been included and there is nothing redundant. The presentation is clear and the booklet is readable. The notes should be of great value to employers of tropical labour in malaria-stricken countries where expert advice and supervision are unavailable—not only in Malaya, for which country the notes were primarily intended.

Norman White.

SIMMONS, S. W. **Progress in the Development of Malaria Control Techniques.** *J. National Malaria Soc.* Tallahassee, Fla. 1946, June, v. 5, No. 2, 157–63.

HOLLIS, M. D. **Postwar Malaria Control in Continental United States.** *J. National Malaria Soc.* Tallahassee, Fla. 1946, June, v. 5, No. 2, 95–8.

EKZEMPLARSKAYA, E. V. [**Immunity in Experimental Malaria of Monkeys** (*Macacus rhesus*).] *Med. Parasit. & Parasitic Dis.* Moscow. 1946, v. 15, No. 1, 50–53. [25 refs.] [In Russian.]

The author, working with macaque monkeys (*Macacus rhesus*) experimentally infected with *Plasmodium inui*, studied certain aspects of immunity in malaria. Reinfection of monkeys, suffering from chronic malaria, with different strains of *P. inui* showed that they acquired an immunity only against homologous strains but were fully susceptible to infection with heterologous strains of the same species of parasite. Attempts were made to produce passive immunity by injection of serum of monkeys, which had recovered from the disease, before or simultaneously with the inoculation of the parasites. The results were all negative, although the presence of antibodies of low titre (1 : 64) during the early days of the infection (6–10th days) was established by agglutination tests. These experiments show that the humoral factor in the defence mechanism against monkey malaria is insignificant as compared with the cellular factor, manifested by the phagocytic reaction of the reticulo-endothelial system. The

functional disturbance of this system, brought about by splenectomy, intensifies the infectious process and may even bring about a fatal termination. The examination of histopathological material obtained from monkeys at different stages of the disease provides direct evidence of phagocytic reaction throughout the entire course of the infection and emphasizes the importance of hyperfunction of the reticulo-endothelial system in checking the infection.

C. A. Hoare.

MAJUMDER, D. N. & DAS GUPTA, C. R. **Haematological Studies in** *Silenus* (*Macacus*) *rhesus*. **Part I. The Blood Picture of the Normal Monkey. Part II. Nature of Malarial Anaemia in Monkeys.** *Indian J. Med. Res.* 1944, May, v. 32, No. 1, 101–4, 8 graphs & 1945, May, v. 33, No. 1, 161–72, 12 graphs. [16 refs.]

i. In the first paper the authors describe the results of haematological studies on 59 normal *Macacus rhesus*, involving 245 examinations of venous blood drawn from a posterior leg vein into a mixture of ammonium and potassium oxalates. Each sample of blood was examined for haemoglobin, total red cells, cell volume and reticulocytes and in each case the mean corpuscular volume (MCV), the mean corpuscular haemoglobin (MCH) and the mean corpuscular haemoglobin concentration (MCHC) were calculated from the first three data. The technique followed was that described by NAPIER and DAS GUPTA (1942) in their " Haematological Technique ". The detailed results are given in a table together with the earlier findings of RAO and RAO (*Indian J. Med. Res.* 1940, v. 27, 1101) and SHUKERS *et al.* [this *Bulletin*, 1939, v. 36, 424]. Apart from the differential leucocyte count the findings are almost identical with those of Shukers *et al.*, who were observing the same species of monkey. The findings of Rao and Rao differed to some extent, but they were using a different monkey, *Macacus sinicus*. As regards the differential leucocyte count, the authors find that of a mean total of 15,380 leucocytes per cmm. a mean of 48·3 per cent. was neutrophils, 47·9 per cent. lymphocytes, 1·61 per cent. monocytes, 2·2 per cent. eosinophils and an occasional basophil.

ii. In the second paper similar haematological studies were made on one monkey which succumbed in four days to a *P. knowlesi* infection, on three suffering from a subacute infection, and on seven with a chronic infection. In the acute infection there was no appreciable change in the blood until more than 1 per cent. of the red cells were infected. The corpuscular constants showed little change until the last stage was reached, when there occurred a sudden upward turn in the MCV curve. Reticulocytes first showed a marked increase towards the end of the infection. The anaemia developed steadily as the parasite density increased beyond the 1 per cent. level. In the subacute infections brought about by regulated doses of quinine, the anaemia, though developing more slowly, was very similar to that seen in the acute infection. In contrast to the acute infection there was a definite tendency to blood regeneration, as shown by the rise in the reticulocyte curve and the presence of normoblasts in the peripheral blood. In general, the corpuscular constants were little altered. In the chronic infections, also produced by suitable doses of quinine, the anaemia developed still more slowly, while there was a marked tendency to blood regeneration. In these animals death generally resulted from complications other than anaemia.

The authors conclude that the anaemia is characteristically normocytic and orthochromic, with a tendency towards macrocytosis at the lower levels of anaemia. The van den Bergh (indirect) reaction is generally negative except in the terminal stages of an infection. There is a varying degree of reticulocytosis which is related to the degree of anaemia present. *C. M. Wenyon.*

RODHAIN, J. & LASSMAN, P. Le comportement en culture suivant la méthode de Bass des plasmodiums de chimpanzé. [**Behaviour of Chimpanzee Plasmodia in Culture by Bass's Method.**] *Ann. Soc. Belge de Méd. Trop.* 1944, Sept. 30, v. 24, No. 3, 131–45, 1 graph, 1 text fig. & 4 figs. on 1 pl.

By Row's modification of the technique of Bass the authors have attempted culture of the three malarial parasites of the chimpanzee which resemble the three common parasites of man. The most readily cultivated is *P. reichenowi*, which though corresponding closely with *P. falciparum* is no more inoculable to man than *P. falciparum* is to chimpanzees. Schizonts appeared in the culture and liberated their first merozoites in 28 to 31 hours. Later examinations showed that some of these merozoites entered erythrocytes and continued their development to fully formed schizonts and parasites of a third generation. In the case of *P. schwetzi* and *P. rodhaini* (corresponding to *P. vivax* and *P. malariae*) development up to a first schizogony was noted but growth of the resulting merozoites could not be followed. In certain tubes employed for culture human or baboon serum was used instead of chimpanzee serum. In human serum *P. reichenowi* did not grow satisfactorily but both *P. schwetzi* and *P. rodhaini* developed as well in these sera as in that of the chimpanzee, though it is known that *P. schwetzi* will not infect the baboon. A culture of *P. falciparum* from man was successful. It appears that the number of merozoites of *P. reichenowi* (8 to 26) is lower than that of *P. falciparum* (20 to 32, according to J. G. and D. THOMPSON). *C. M. Wenyon.*

BRUMPT, E. & DAO VAN TY. Essais négatifs de conservation par le froid (—25°C.) des schizontes, des gamètes et des sporozoïtes de *Plasmodium gallinaceum*. [**Negative Attempts to preserve** *P. gallinaceum* **at —25°C.**] *Bull. Soc. Path. Exot.* 1945, v. 38, Nos. 11/12, 323–6.

The authors record experiments in which blood and mosquitoes infected with *P. gallinaceum* were rapidly frozen to —25°C. and maintained at this temperature for some weeks with the object of testing the survival of the parasites at low temperatures. The survival was tested by bringing the blood or mosquitoes to 37°C. and, when thawing had taken place, inoculating young chicks. In no case, however, did infection occur. The authors record the negative result in order to save others from wasting their time in a similar fruitless endeavour. *C. M. Wenyon.*

TONKIN, Isabel M. **The Testing of Drugs against Exoerythrocytic Forms of** *P. gallinaceum* **in Tissue Culture.** *Brit. J. Pharmacol.* 1946, Sept., v. 1, No. 3, 163–73, 1 fig.

In these tests the minced spleens of chickens heavily infected with the tissue phase of *P. gallinaceum* were cultured in a sterile fluid medium consisting of Tyrode's solution, chicken serum and embryo extract as described by HAWKING [this *Bulletin*, 1946, v. 43, 410]. Changes in the *p*H of the medium, which was replaced every 5 to 6 days, were indicated by dilute phenol red, and a small concentration of penicillin prevented the growth of bacterial contaminants. The drugs for test were dissolved in sterile Ringer's solution at various dilutions before being added to the culture medium. Some reduction of drug concentration resulted from absorption by tissues present. When after 7 to 10 days' incubation at 37°C. parasite development was satisfactory in the control flasks, specimens were withdrawn on coverslips from the experimental flasks and examined after staining. The absence of viable parasites in the flasks containing the drug was confirmed by inoculation of culture material from them into chickens, and noting whether infection resulted. Thirteen drugs of varied constitution

were tested by this technique, which is elaborate and in a number of cases proved unsatisfactory on account of the toxicity of the drugs for macrophages, as well as their insolubility in the medium. Several sulphonamides, streptomycin, streptothricin and *p*-anisylguanidine nitrate inhibited parasite growth and were non-toxic to macrophages. Inhibition of sulphathiazole activity was prevented by *p*-aminobenzoic acid, but not that of a *m*-sulphonamide by *m*-aminobenzoic acid. Sulphathiazole inhibited division of the parasite in developed cultures, an effect already described by BRACKETT *et al.* [this *Bulletin*, 1946, v. 43, 411] on exoerythrocytic forms in the chick host.

J. D. Fulton.

SEELER, A. O. & OTT, W. H. **Effect of Deficiencies in Vitamins and in Protein on Avian Malaria.** *J. National Malaria Soc.* Tallahassee, Fla. 1946, June, v. 5, No. 2, 123–6, 1 fig.

" Parasite counts in *P. lophurae* infections in well-nourished chicks were less than in infected chicks deficient in biotin, folic acid or protein. On the other hand the parasitemia was less in chicks deficient in riboflavin than in the well nourished chicks. In the case of thiamine, the parasitemia appeared to be lower in chicks receiving approximately the minimal dietary requirements for normal growth than in either severely deficient chicks or in chicks given excess thiamine. Parasitemia in chicks fed a diet of natural foodstuffs was lower than in chicks given purified diets complete in all recognized nutrients."

TRYPANOSOMIASIS.

IKEJIANI, O. & MAUTNER, L. S. **Changes in the Leucocyte Picture in Experimental Trypanosomiasis by Administration of Neostibosan and Neostam.** *J. Pharm. & Exper. Therap.* 1946, Aug., v. 87, No. 4, 343–9, 4 figs. [14 refs.]

" 1. In rats which show no resistance to infection with *Trypanosoma equiperdum*, the most characteristic change in the leucocyte picture is a decrease in lymphocyte per-centage, increase in polymorphonuclear neutrophil per-centage and a decrease in monocyte per-centage.

" 2. Rats infected with *T. equiperdum* and treated with neostibosan or neostam showed increased monocyte per-centage, decreased polymorphonuclear neutrophil per-centage and increased lymphocytes, after treatment.

" 3. It is suggested that the increased monocytes play adjunctive role in respect to the drugs (neostibosan and neostam) by completing the destruction of trypanosomes after they have been rendered vulnerable by the drugs."

SCHNITZER, R. J., LAFFERTY, Lillian C. & BUCK, M. **The Role of Antibodies in Experimental Drug Resistance of** *Trypanosoma equiperdum*. *J. Immunology.* 1946, Sept., v. 54, No. 1, 47–57. [10 refs.]

In order to investigate the rôle of antibodies in the development of drug-resistance by *Trypanosoma equiperdum*, three different methods were adopted for producing resistance. The chemotherapeutic agent used, throughout the work, was pararosaniline hydrochloride (*i.e.* parafuchsin). This compound exercises a considerably higher activity in infections in rats than in mice. It should, therefore, be especially suitable for the studies in view, since the assumption is that its superior effect in rats is connected with the fact that, as the authors were able to show, these animals exhibit a better immune response

than mice to infections with *T. equiperdum.* Studies in rats may thus be expected to amplify, and not merely to duplicate, the lessons learnt from studies in mice.

The three methods used for producing resistance were as follows (for technical details and actual dosages, etc., the original should be consulted) :—

(*a*) *The relapse method.*—This is the classical method of Ehrlich. It consists in the administration of a dose sufficient to remove trypanosomes from the peripheral blood temporarily. When a relapse occurs, another dose is given, and so on, successive relapses being treated by slightly higher and higher doses, as resistance seems to be developing. Since every relapse is preceded by antibody-formation, the trypanosomes acquiring drug-resistance necessarily do so whilst in the presence of large amounts of antibodies.

(*b*) *The short passage method.*—Heavy infections are treated with very small doses, and the parasites are transferred to new hosts within the next 4 to 8 hours. Each succeeding passage is carried out in this same manner, the dosage being increased step by step. The object is to ensure that the trypanosomes escape the influence of antibodies, by passaging them before the latter have time to appear.

(*c*) *Splenectomy method.*—Animals are infected the day after splenectomy, daily treatment being started within the next 24 hours. Here again the aim is to minimize the influence of antibodies, in this case because of their attenuation as a result of the splenectomy.

In mouse infections, it was found that resistance developed more readily when the immune response was curtailed, *e.g.* by using the short passage, or the splenectomy method, instead of the "classical" relapse method. In rat infections, however, which are characterized by a more abundant antibody formation, the short passage and the splenectomy methods had to be combined in order to obtain resistance consistently within a reasonable time. These findings seemed to indicate that antibodies exercise a definite inhibiting effect on the development of resistance to the compound used. The authors claim further support for this conclusion in experiments which show that passive immunization with trypanocidal antiserum impairs the facility with which resistance may be produced in mice by the splenectomy method.

The interesting note is added that a similar phenomenon has been observed with pneumococci. A strain of these bacteria could ordinarily acquire resistance to sulphapyridine *in vivo* quite easily, but no such resistance developed if the compound was administered in conjunction with subeffective doses of type-specific antiserum. *E. M. Lourie.*

LEVADITI, C. & VAISMAN, A. Transformation de l'atoxyl en trypanotoxyl. [**Transformation of Atoxyl into Trypanotoxyl.**] *Bull. Soc. Path. Exot.* 1946, v. 39, Nos. 7/8, 276–83.

It is now nearly 40 years since the senior author first wrote on this subject. Together with YAMANOUCHI he showed that atoxyl, which is practically non-trypanocidal *in vitro,* can be rendered highly trypanocidal by contact with extracts of liver and other tissues (LEVADITI & YAMANOUCHI, *C. R. Soc. Biol.,* 1908, v. 65, 23). Activation of atoxyl by these means was described as being due to the transformation of that substance into what the authors designated as trypanotoxyl, which they believed to be a reduced form of atoxyl in combination with protein.

Quite recently DUREL and RATNER (*C. R. Soc. Biol.,* 1944, v. 138, 402) have reported inability to confirm this early work. Extracts of fresh liver, and especially of liver which had been kept at room-temperature or at 37°C., did not activate atoyxl but were found to be possessed of trypanocidal properties

on their own account. Levaditi and Vaisman decided, therefore, to re-examine the subject. They have confirmed the original observation that fresh rabbit liver extract, which alone is harmless to trypanosomes (*T. equiperdum*), does in fact render atoxyl trypanocidal *in vitro*. This property is retained for 14 days by extracts from livers kept at —20°C., and for 2 to 4 days by extracts from livers kept at 4°C. In the absence of atoxyl, such preparations exhibit no trypanocidal properties up to the observation periods of 14 days and 7 days, respectively. However, livers kept at room-temperature (20°C.) acquire a trypanocidal property within 2 days, as autolysis develops, the potency of this trypanocidal function increasing up to 7 days, the limit of observation. The trypanocidal activity thus arising supplements that due to activation of atoyxl, when extracts prepared from such livers, after keeping at 20°C. for periods up to four days, are brought into contact with the drug. The liver autolysis proceeds either under sterile conditions, or with the appearance of bacteria, in particular a Pasteurella, and the authors have found that not only this organism but also *Bact. coli* and staphylococci are capable of lysing trypanosomes *in vitro* at 37°C. The authors therefore explain Durel and Ratner's results by supposing that they worked not with fresh livers but with preparations which had already autolysed, either in the absence or in the presence of bacteria.

The trypanocidal factors in autolysed liver are somewhat more thermolabile than the atoyxl-activating components of fresh liver ; the former are destroyed, whilst the latter are only slightly affected, by heating to 100°C. for 30 minutes. Three reducing substances were tested for atoxyl-activating properties, and two, namely glutathione [see this *Bulletin*, 1929, v. 26, 579] and cysteine, were active, whilst the third, ascorbic acid, was not. Hydrogen peroxide also was inactive in this respect. *E. M. Lourie.*

TORREALBA, J. F. Investigaciones sobre Enfermedad de Chagas en Zaraza (Estado Guárico, Venezuela). Otras Notas Cientificas. Recopilación. [**Studies in Chagas's Disease in Zaraza, Guárico State, Venezuela, and other Collected Papers.**] Fascículo 1°. 1943. 168 pp., 17 figs. Caracas : Litografia del Comercio & Fascículo 2°. 1946. 256 pp., 33 figs. Caracas : Tipografia Garrido.

In these two volumes Dr. Torrealba has collected together his papers on various subjects published during the decade 1932–1942. Most of them deal with Chagas's disease and all have been published before ; most of them are already known to readers of this *Bulletin* ; in short, they form a collection of reprints. Of most of them Dr. Torrealba was the sole author, but a few have been the result of collaboration. A list is given of those making up the first volume, but there is none of the second group. This is a pity because it is tedious to wade through 250 odd pages to look for some point which has escaped one's memory. It is difficult to say exactly what niche these volumes will fill, or what purposes they are designed to serve, except as a record of much once useful work gathered from various sources, or as a kindly gesture for the author to give his friends.

In the first volume are 11 papers on Chagas's disease, dealing with the clinical, diagnostic and therapeutic aspects ; also one on leprosy in Zaraza in 1936 ; others on parasitology (1932), psychiatry (1924), obstetrics (1937) and malignant growths (1930). In the second volume are ten more papers dealing with some aspect of Chagas's disease, a list of the 10 genera of the Triatomidae Family and 78 species. Twenty-six species are found infected in nature ; these, too, are listed, together with the names of those who first reported their discovery ; 7 others experimentally infectable are named and a list is given of ten

species found in Venezuela. These are *Triatoma dimidiata, T. nigromaculata, T. rubrofasciata, Eutriatoma maculata, Erathyrus cuspidatus, Belminus rugulosus, Panstrongylus geniculatus, Psammolestes arthuri, Rhodnius pictipes* and *R. prolixus.*

Other papers include one of brief remarks on some studies carried out on pathological specimens collected in 1943—bloods for *T. cruzi* and malaria, snails (mainly *A. glabratus*) depicted on 4 plates, and spleen pulp specimens. Another contribution consists of brief notes of 60 cases seen in a malaria outbreak in Zaraza in 1941 ; 18 were *P. vivax* infections, 36 *P. falciparum*, 3 *P. malariae*, one a mixed *P. vivax* and *P. falciparum*, and two not decided. Another paper is concerned with the clinical forms of cancer in Zaraza and there is one, reprinted from *Gaceta Médica de Caracas* 1943, on the medical zoology of the district.

From the above account it will be gathered that most of the information is mainly of local interest and much of it, though important when the papers were published, has, with the lapse of time, lost a good deal of its value. Anyway, these two volumes constitute a record of much good work done.

H. Harold Scott.

LEISHMANIASIS.

MALAMOS, B. **Leishmaniasis in Greece.** *Proc. Roy. Soc. Med.* 1946, Oct., v. 39, No. 12, 799–801, 7 figs.

See this *Bulletin*, 1947, v. 44, 1.

PEREIRA, C. & MEDINA, H. Viragem da coloraçâo por uma laca férrea da hemateina pela prata amoniacal, para o estudo das leishmanias, principalmente nos tecidos. [**Toning in Ammoniacal Silver of Staining by an Iron Haematin Lake, for the Study of Leishmania, specially in the Tissues.**] *Arquivos Inst. Biologico.* São Paulo. 1945, v. 16, 41–8, 2 figs. on 1 pl. [12 refs.] English summary.

" After trying many techniques for the study of Leishmania in the tissues, the following is proposed.

" Staining solutions :

" 1. Ferric chloride, U.S.P., XII solution, aqueous dilution to 10 per cent.

" 2. Picric acid, saturated solution in 75–76 per cent. ethyl alcohol.

" 3. Sodium thiosulphate, aqueous solution, 2 per cent.

" 4. Hematein solution : hematein, 10 per cent. in alcohol-glycerin mixture—10 ml. ; 95–96 per cent. alcohol—60 ml. ; 1 per cent. ammoniacal solution—20 ml. ; tannin, 20 per cent. aqueous solution—10 ml.

" 5. Ammoniacal silver : to a 10 per cent. aqueous solution of silver nitrate, add ammonia drop by drop, shaking well until the precipitate is just dissolved ; dilute the solution to 0·5 per cent. silver nitrate.

" Method of staining.

" 1. Mordant sections in the ferric chloride, 1 minute or longer.

" 2. Stain in the hematein, on the slide, 3 minutes or longer.

" 3. Rinse in water, and differentiate in the alcoholic picric acid, 0·5 minute or longer.

" 4. Rinse in water, and tone on the slide in the ammoniacal silver solution, 5 minutes or longer.

" 5. Rinse in water, and fix in the sodium thiosulphate solution, 1 minute or longer.

" 6. Wash in water, dehydrate, clear and mount in balsam.

" Results.—Chromatin, nucleoli, centrioles, kinetic apparatus of the flagellates and certain parts of striated muscle fibres are stained black; cytoplasm greyish; red blood cells bluish. The Leishmania are easily visible with the high dry power and sharply defined with the oil immersion lens."

DHARMENDRA, BOSE, R. & SEN GUPTA, P. C. **The Preparation of an Antigen from the Kedrowsky's Bacillus for the Complement-Fixation Test for Kala-Azar.** *Indian J. Med. Res.* 1946, May, v. 34, No. 1, 1–2.

In an earlier paper [this *Bulletin*, 1941, v. 38, 702] the authors pointed out that for the preparation of the W.K.K. antigen for the complement fixation test in kala azar, in place of tubercle bacilli, other and more readily cultivated acid-fast bacilli, such as that of Kedrowsky, could be used. In the present paper details of the method of preparation of the antigen are given.

The growth from a three weeks' culture of Kedrowsky's bacillus on glycerin broth is filtered off and washed on the filter paper with distilled water and rectified spirit. The residue is dried *in vacuo* in a desiccator. The dried product is extracted with 90 per cent. alcohol for three hours in a flask fitted with a reflux condenser over a water bath, filtered free from alcohol and again dried *in vacuo*. The dried alcohol-insoluble residue is then extracted with pyridine for eight hours at a temperature of 135°–140°C. in a Soxhlet apparatus over a glycerin bath. The pyridine extract is evaporated to dryness in a dish over a hot air bath at 70°C. The dry pyridine extract is next extracted for two hours with acetone in a Soxhlet apparatus over a water bath. The insoluble residue, when dried, is the antigen. The quantity of antigen obtained is about one-tenth of the weight of the original dried bacillary mass. For use, 0·1 gramme of the antigen is dissolved in 10 cc. benzol and to it is added the residue obtained by evaporating to dryness 5 cc. of a 1 per cent. solution of lecithin. This is the lecithinized benzolic solution of the antigen which is used in the test. It is kept in the incubator at 37°C. for 10 to 15 days before use. *C. M. Wenyon.*

BOSE, B. C., IYENGAR, N. K. & MUKERJI, B. **On the Assay of Urea Stibamine.** *Indian J. Med. Res.* 1945, May, v. 33, No. 1, 151–6, 2 graphs. [10 refs.]

As the antimony content of different batches of urea stibamine varies considerably, and, as GRAY and others have pointed out, the drug is not a compound of uniform formula, it is difficult to set up a standard in order to control the various preparations issued for clinical use. However, the authors have attempted to do this by selecting a batch (No. 0596) manufactured at the Brahmachari Institute in Calcutta as a temporary standard. They have determined its chemical composition and worked out in white mice a dose-response curve. The LD_{50} figure was found to be 215 mgm./kgm. for white mice of 18 to 20 gm. weight. It is suggested that a maximum variation of ± 30 per cent. on this figure be permitted. Solutions of urea stibamine are much more stable than organic arsenicals, so that it is unnecessary to take the elaborate precautions in the preparation of solutions, which the arsenicals require. As the relationship of total antimony content of urea stibamine to its toxicity is unknown, and as there is no indication which fraction of the drug is therapeutically active, for the present the assay of preparations of the drug must be carried out by biological methods. *C. M. Wenyon.*

HO, E. A. **Treatment of Kala Azar by Small Dosage of Ureastibamine.** *Chinese Med. J.* (Chengtu Edition.) 1944, Oct., v. 63A, No. 1, 7–11.

With a view to avoiding the toxic symptoms which not infrequently result from the treatment of kala azar with urea stibamine, the authors have investigated the possibility of employing smaller doses than is customary. It was

found that when individual doses were limited to 0·03–0·05, 0·05–0·75 and 1·0 to 1·5 gm. for infants, children and adults respectively, toxic symptoms rarely occurred. With these doses employed in 160 cases the only symptoms were mild and transient nausea and vomiting which were experienced by five patients after the fourth dose. The doses were administered either once a week or twice a week for six weeks, six or twelve injections in all. The average total dose was 0·03 gm. per kilo. of body weight for children and 0·02 gm. per kilo. for adults. It is concluded that with a weekly dose for six weeks the great majority of cases will be cured. The advantage of this type of treatment in field work is that a health worker can do a round of seven clinics in a week without any fear of the drug causing the development of serious toxic symptoms.

C. M. Wenyon.

HARRISON, C. V. & FULTON, J. D. **The Effect of Treatment on the Spleen of the Golden Hamster** (*Cricetus auratus*) **infected with** *Leishmania donovani.* *Brit. J. Exper. Path.* 1946, Feb., v. 27, No. 1, 4–8, 2 figs.

A series of 72 golden hamsters were used to study the effect of *Leishmania donovani* infection on the spleen and the response of this organ and the infection to treatment with 2-hydroxy stilbamidine which was administered intraperitoneally on alternate days—ten doses of 20 mgm. per kilo. of bodyweight. The earliest histological change in untreated animals is an overgrowth of the reticulum cells of the germinal centres of the Malpighian bodies, causing them to enlarge. This enlargement reaches a maximum in four to six weeks. In the pulp the first change is a slight diffuse proliferation of the reticulum cells, followed by a transitory phase of congestion lasting from the fourth to the eighth week. After the sixth week there is a progressive proliferation of the reticulum cells. This commences in small foci which enlarge and become confluent so that the blood is crowded out, leaving an almost completely cellular pulp. Leishmania were present in all cases. They increased in number up to 12 weeks and then declined, but remained above 100 per field. They occurred in the foci of hyperplasia in the malpighian bodies and pulp. In treated animals there is a rapid reduction in the size of the spleen from a weight of 350 to 575 mgm. to one of about 300 mgm. This takes place during the first half of the course of treatment and, though with completion of the course the leishmania infection is eradicated, further reduction in the size of the spleen does not occur. This persisting splenomegaly above the normal weight of 81 mgm. is not due to cellular hyperplasia or congestion but is caused by a general enlargement of the organ which takes place during the active phase of infection. The histological changes are similar to those occurring in the human spleen during infection with *L. donovani.* *C. M. Wenyon.*

KERVRAN, P. Description de quelques espèces de phlébotomes du Soudan français. [**Description of Species of** *Phlebotomus* **from the French Sudan.**] *Ann. Parasit. Humaine et Comparée.* 1946, v. 21, Nos. 3/4, 155–65, 4 figs.

The author re-describes *P. roubaudi* Newst. which seems to be common at Timbuctoo, Gao, etc. The adults appear in the rains (June to November) and bite man. This species is probably the transmitter of cutaneous leishmaniasis which is widespread, though not common, in the French Sudan.

Detailed systematic notes are given on several species. *P. A. Buxton.*

GILL, S. **Cutaneous Leishmaniasis (Oriental Sore). Report of Autochthonous Cases observed in Haifa.** *Arch. Dermat. & Syph.* 1946, Sept., v. 54, No. 3, 333–7, 5 figs.

ANSARI, N. Quelques procédés concernant l'utilisation de la pénicilline dans l'isolement de *Leishmania tropica*. [**Use of Penicillin for isolating** *L. tropica*.] *C. R. Soc. Biol.* 1945, Oct., v. 139, Nos. 19/20, 897–8.

When material from an oriental sore is inoculated to N.N.N. medium for the purpose of culturing *Leishmania tropica* there is always the possibility that contaminating bacteria will outgrow the leishmania. The author has found that cultivation at 15°C. keeps the bacteria in check, while still permitting the leishmania to become flagellates and multiply. In many cases after a number of subcultures at this temperature, pure cultures of the flagellates were obtained. More satisfactory results were obtained, however, by adding to the culture medium sufficient penicillin to give a concentration of 1,250 units per cc. In this medium, bacterial growth is insignificant so that pure cultures of leishmania are regularly obtained after two or three subcultures. It was found that stronger concentrations of penicillin hindered the growth of the leishmania.

C. M. Wenyon.

FEVERS OF THE TYPHUS GROUP.

MOOSER, H. **Twenty Years of Research in Typhus Fever.** *Schweiz. med. Woch.* 1946, v. 76, Nos. 37/38, 877–82. [71 refs.]

This interesting paper is a summary of the recent book, published in German, by the same author, on the relationship between murine and classical typhus [this *Bulletin*, 1946, v. 43, 611]. Although it deals with only certain aspects of the subject, medical historians will find it helpful in correcting some misunderstandings which still persist in connexion with the early work on murine typhus.

Most of the numerous statements of facts contained in the paper are documented, but a few points are open to criticism. For example, the opening words of the paper are:—"Up to 1926 typhus had been regarded by all European students as a well-defined morbid entity with respect to its epidemiology. . . . ." Unless British observers are excluded from the term "all European students" this statement is not correct. Many years before 1926, SAMBON held that the Rocky Mountain spotted fever was a form of typhus; in 1917 the reviewer suggested that the tick-borne and mite-borne typhus-like fevers should be regarded as belonging to the "typhus group of fevers," and in 1921 he proposed the provisional names, "louse typhus", "tick typhus", and "mite typhus". It cannot be said that these diseases belonged to "a well-defined morbid entity" in respect of their epidemiology.

In the next paragraph the author mentions the "pseudo-typhus of Delhi": presumably he refers to the disease described by SCHÜFFNER in a paper in English as "pseudo-typhoid" occurring in Deli in Sumatra. In papers in German, Schüffner naturally used the name "pseudo-typhus" which in English means pseudo-typhoid, because it refers to typhus abdominalis, which German writers constantly call "typhus".

The author also suggests that in 1929 the causative agent of louse-borne typhus was still unknown; but surely by that date the majority of workers on typhus had come to accept *Rickettsia prowazeki* as the cause, despite the extraordinary statement, quoted by the author from a report dated December 1929 of the Health Committee of the League of Nations, in which the following words occur "the causative agent has never been discovered."

The important part played by the author in typhus research is fully recognized, as is shown by the current use of the names *Rickettsia mooseri*, the

Neill-Mooser reaction, and Mooser's cells ; the brilliance of his discoveries needs no enhancement by painting the prevailing ignorance in 1929 of the cause and relationships of classical typhus in unduly sombre colours.

John W. D. Megaw.

LEMIERRE. **Note on Localised Epidemics of Exanthematic Typhus amongst Prisoners of War in France.** *Bull. Office Internat. d'Hyg. Publique.* 1946, Apr.–May–June, v. 38, Nos. 4, 5 & 6, 259–63.

During the months of August and September 1945, no cases of typhus fever were detected in France, but in October and November outbreaks occurred among German prisoners of war, (1) in the Bordeaux area where 195 proved cases with 47 deaths occurred, and (2) in the Marseilles area where there were 33 cases with 2 deaths. Only a few cases occurred among the camp guards and French civilians who came into contact with the patients. Both outbreaks were promptly controlled by isolation, vaccination, and disinfestation.

In the absence of any evidence of a recent influx of infected persons the outbreaks are regarded as " a local reappearance of the disease among persons of low resistance."

John W. D. Megaw.

BULL. OFFICE INTERNAT. D'HYG. PUBLIQUE. 1946, Apr.–May–June, v. 38, Nos. 4, 5 & 6, 253–4. **Exanthematic Typhus in Tunisia from 1939 to 1946.**

The monthly incidence of louse-borne typhus in Tunisia since 1939 is shown in a table from which it appears that the largest number of cases reported in one month in 1939 and each of the succeeding years was :—1929, 1,098 (in April) ; 1940, 895 (May) ; 1941, 1,058 (May) ; 1942–3, 138 (March) ; 1943, 1,242 (March) ; 1944, 156 (May) ; and 1945, 44 (January).

The lowest monthly incidence in each year was in September or October, except in 1944, when it was in August.

The comment on the figures is :—" During the winter months of 1944–1945 and 1945–1946 there was a general state of calm ; the only rational explanation of this calm lies most certainly in the repeated and large-scale vaccination of all classes of the Tunisian population."

[The natural tendency of epidemics to wax and wane is not mentioned.]

John W. D. Megaw.

PADILLA B., E. Las rickettsiasis en Guatemala. [**Rickettsial Disease in Guatemala.**] *Bol. Oficina Sanitaria Panamericana.* 1946, June, v. 25, No. 6, 519–24, 1 map & 2 charts. [Summary in English by the author.]

" With the results of more than a thousand complement fixation tests in which epidemic and murine antigens prepared by the Army Medical School of Washington were used, and with due control of the tests, it may be inferred that typhus in Guatemala is of the epidemic type in more than 95 per cent. of the cases and in the remainder murine or endemic. Constant and significant agglutinations were obtained only with Proteus OX19. OX2 and OXL strains do not agglutinate with the sera of the above-mentioned cases. No cross-agglutinations have ever been obtained with brucellas. A positive complement fixation test was found in one case with a history of typhus 35 years before. For any investigations of rickettsial infection, it seems essential to combine use of the Weil-Felix and the complement fixation tests. The development of both reactions is almost simultaneous during the first week in which the symptoms appear. Several tables and one map are included to show the distribution, incidence and mortality of typhus in Guatemala in 1934–1944."

HEIDE, E. A. Der mikroskopische Nachweis der Rickettsia Prowazeki im Blutausstrich von Fleckfieberkranken. [**Microscopical Demonstration of *Rickettsia prowazeki* in Blood Smears from Typhus Patients.**] *Zent. f. Bakt.* I. Abt. Orig. 1944, July 12, v. 151, No. 6, 289–93, 5 figs.

Stained blood smears of about 200 patients were examined on the 10th to the 12th day of severe attacks of louse-borne typhus fever; in eight of these, bodies were found which had all the appearances of rickettsiae.

In most of the cases the bodies were bacilliform, but in one they were coccoid and in another the appearance was suggestive of an endothelial cell densely packed with rickettsiae.

Five reproductions of photomicrographs illustrate the article, and they certainly appear to justify the author's view that rickettsiae can occasionally be seen in blood films from patients suffering from severe attacks of typhus fever. *John W. D. Megaw.*

D'IGNAZIO, C. Le complicanze del dermotifo. [**The Complications of Typhus.**] *Bol. Soc. Ital. di Med. e Igiene Trop.* (Sez. Eritrea.) 1946, v. 6, Nos. 1/2, 97–105. [Summary in English by the author.]

"The more common complications of typhus in Ethiopia are described by the author as well as the rarest."

D'IGNAZIO, C. & CODELEONCINI, E. La prognosi nel dermotifo. [**The Prognosis of Typhus.**] *Bol. Soc. Ital. di Med. e Igiene Trop.* (Sez. Eritrea.) 1946, v. 6, Nos. 1/2, 53–68.

STUART, G. **The Typhus-Relapsing Fever Association.** *Epidemiological Information Bull.* (UNRRA Health Division). Washington, D.C. 1946, v. 2, No. 16, 665–74.

The author discusses the degree to which epidemics of the louse-borne types of typhus and relapsing fever are associated with each other in time and place.

(1) Epidemics of louse-borne typhus may occur in the absence of epidemics of louse-borne relapsing fever, as in Germany between 1941 and 1946, in Algeria in 1920–1923, in Tunisia in 1937, in Morocco in 1928, and in Poland in 1945–1946.

(2) Epidemics of relapsing fever may also occur in the absence of epidemics of typhus; for example the epidemic of relapsing fever, which started in French West Africa in 1921, swept through the French Sudan and Anglo-Egyptian Sudan, and was finally arrested in 1927. Another example was the epidemic of relapsing fever in Kenya in 1945 and 1946.

[Between 1917 and 1924 relapsing fever in severe epidemic form swept over large areas of India in which epidemics of typhus had never been known to occur. The available evidence suggests that relapsing fever can establish itself in some hot countries in which typhus fever is not easily transmitted.]

(3) When epidemics of typhus and relapsing fever have been related to each other in the same areas there has usually been a time-lag between the commencement of the typhus epidemic and that of the epidemic of relapsing fever. During the years 1941 to 1946, epidemics of typhus and relapsing fever have occurred in Egypt, Tunisia, Algeria, French Morocco, and Rumania; in each case typhus appeared in epidemic form three or four years before relapsing fever, and in all these countries except Rumania there was a similar time lag between the peaks of the epidemics.

In the great epidemics in Russia during 1919 and 1920 typhus became intensely prevalent a year earlier than was the case with relapsing fever, though the peak year of prevalence of the two diseases was 1920.

In associated epidemics of these diseases, relapsing fever tends to subside more rapidly than typhus. *John W. D. Megaw.*

WISHART, F. O. & MALCOMSON, M. Elizabeth. **Studies of the Serology of Typhus Fever.** *Canadian J. Pub. Health.* 1946, Sept., v. 37, No. 9, 369–81, 1 fig. [17 refs.]

The authors have studied the properties of the complement-fixing antigens of epidemic and murine typhus rickettsiae and of *Proteus OX19*, with special reference to the heat-stable antigens whose presence in *Rickettsia prowazeki* and many other organisms had already been demonstrated.

In the present study, antigens were prepared in various ways from two strains of *R. prowazeki*, from the Castañeda strain of *R. mooseri*, and from *Proteus OX19*; these were used in fully-controlled complement-fixation tests of sera of guineapigs immunized by each type of antigen. Quantitative absorption tests were also carried out in which known amounts of rickettsial suspensions were used.

It was found that each of the two rickettsiae, *R. prowazeki* and *R. mooseri*, contained a type-specific antigen labile at 60°C. and a common antigen stable at 100°C. but destroyed at 120°C. By absorption tests it was shown that the stable antigen contained two factors, one of which was common to *Pr. OX19*, while the other was present only in the rickettsial strains. *Pr. OX19* in turn possessed a second factor " concerned with reactions in proteus antiserum but not in anti-typhus serum." From this observation the authors conclude that " The presence of an antigen common to *R. prowazeki* and *Pr. OX19* indicates that the Weil-Felix reaction is a specific immunological reaction."

The original article must be consulted for details of the methods of preparing the rickettsial suspensions and carrying out the various tests.

John W. D. Megaw.

HAMMARSTRÖM, E., FAHRAEUS, J. & HELLSTEN, M. D. H. **Research on the Weil-Felix Reaction and the Specific Agglutination of Rickettsias in Patients suffering from Exanthematic Typhus.** *Bull. Office Internat. d'Hyg. Publique.* 1946, Apr.–May–June, v. 38, Nos. 4, 5 & 6, 270–73.

The authors carried out Weil-Felix and rickettsia-agglutination tests on the sera of about 200 typhus patients who were refugees from German concentration camps.

The rickettsia-agglutination test was carried out by the technique of Packalen, who, according to the authors, " seems to have been the first to attempt the specific agglutination of Rickettsias and the fixation of the alexin on a sufficiently large scale." The rickettsial suspensions were prepared from yolk-sac cultures by differential centrifugation; the readings were made after the test dilutions had been kept for four hours in the incubator at 37°C. and through the night at laboratory temperature. A droplet of the lowest layer of each dilution was placed on a slide, dried in air, stained with cyanosine, and examined microscopically. The presence of even the smallest clumps was regarded as showing a positive reaction.

The suspensions of *Proteus OX19* were treated with alcohol and ether by Gard's method; they were dried, ground in a mortar, and stored in tubes with rubber stoppers. In this form the test material kept well for at least six years. Readings were made after 24 hours in the incubator.

Using these methods the authors found that about half of the patients reacted with the rickettsia-agglutination test at a titre of 1–81,920, and with the Weil-Felix test at a titre of 1–320 by the 8th or 9th day. These titres were taken as indicating positive reactions; in 22 cases the rickettsia test was positive and the Weil-Felix negative; in six cases the Weil-Felix was positive and the rickettsia negative.

The detailed results are shown in tables; there was a general degree of correspondence between the results in the two tests, but the rickettsia test was regarded as being more sensitive and reliable. *John W. D. Megaw.*

MEYER, R. Gibt es eine für die Fleckfieberdiagnose bedeutungsvolle Reifung der agglutinatorischen Kraft im Sinne Schroers? [**Has the Ripening of the Agglutination Reaction the Significance in the Diagnosis of Typhus Fever claimed for it by Schröer?**] *Zent. f. Bakt.* I. Abt. Orig. 1944, July 12, v. 151, No. 6, 302–7.

The author refutes the claim made by SCHRÖER [see this *Bulletin*, 1945, v. 42, 545] that when the titre of the Weil-Felix reaction is observed after two hours' incubation and again after 22 hours at room temperature the rise in titre between the two observations is much greater in cases of typhus fever than in false-positive reactions due to other conditions.

Evidence is produced to show that the rise in titre is purely a "time function" independent of any differences in the quality of the agglutinins concerned.

The author gives a list of conditions that must be fulfilled before a titre of 1–400 after 15–18 hours' incubation can be accepted as significant; these include the absence of (1) icterus or hepatitis, (2) recent typhus vaccination, and (3) *Proteus X19* infection.

The paper will be found interesting by students of the Weil-Felix reaction. *John W. D. Megaw.*

OLITZKI, L., CZACZKES, J. W. & KUZENOK, A. **Endotoxic Factors of *Rickettsia prowazeki* and their Immunological Relationship to the Endotoxins of other Gram Negative Microorganisms.** *J. Immunology.* 1946, Aug., v. 53, No. 4, 365–70.

Olitzki *et al.* have already shown that rickettsial vaccines heated for two hours at 100°C. contain toxins which, when injected into white rats, produce effects similar to those produced by other Gram-negative organisms; the effects include a fall of temperature and a lowering of the glycogen content of the liver.

In the present experiments it was found that rats, after immunization by heat-killed vaccines made from *Rickettsia prowazeki*, or *Proteus X19*, or *Shigella dysenteriae*, no longer showed toxic effects after injections of epidemic-typhus vaccine. No specific difference was detected between the immunizing power of the three vaccines.

So also it was found that rats immunized by the endotoxins of *R. prowazeki* were as resistant to the endotoxins of *Pr. X19* and *S. dysenteriae* as they were to the endotoxins of *R. prowazeki*.

The authors conclude that the endotoxic factors of *R. prowazeki* are possessed in common by certain Gram-negative organisms, and confer a "factor-specific" immunity against the endotoxins of these organisms, which, therefore, are immunologically related to *R. prowazeki*.

The bearing of these findings on the classification of the rickettsiae is discussed; these organisms obviously contain a toxic product which is a common constituent of a large group of Gram-negative bacterial organisms.

John W. D. Megaw.

OLITZKI, L. & BUECHLER, E. **Studies on the Detoxication of the Labile Rickettsia Toxin.** *Brit. J. Exper. Path.* 1946, Aug., v. 27, No. 4, 220–24.

The authors have confirmed the findings of KLIGLER and OLEINIK [this *Bulletin*, 1945, v. 42, 23] who showed that yolk-sac cultures of *Rickettsia prowazeki* and *R. mooseri* contain labile toxins which are present in the supernatant fluid after centrifugation. Evidence of the presence of these toxins included splenic enlargement in 14–day-old rats to which suitable doses were given by the intraperitoneal route.

In the present experiments it was found that the toxins passed readily through Mandler and Seitz filters.

The toxins were readily detoxicated by formalin, permanganate of potassium or bisulphite of sodium ; rats inoculated with the resultant toxoids were found immune to the effects of the original toxins. [In the original paper, the wrong reference is given to Kligler and Oleinik's paper.] *John W. D. Megaw.*

SADUSK, J. F., JR. & KUHLENBECK, H. **Dangers associated with the Use of Living "Attenuated" Typhus Vaccine.** *Amer. J. Pub. Health.* 1946, Sept., v. 36, No. 9, 1027–30. [22 refs.]

A translation is given of an official Japanese report dealing with an incident that happened during an epidemic of louse-borne typhus in Hokkaido, Japan.

Members of the staff of the Kitasato Institute (Tokyo) inoculated more than 11,000 persons in Hakodate during May and June 1944, with a living bile-attenuated vaccine made from *Rickettsia mooseri*. The only reaction observed was mild headache, which affected about 10 per cent. of the persons inoculated.

Without obvious reason, about 70 per cent. of one group of 290 persons, inoculated in the same way, developed fever, which lasted about 14 days and was associated with a strongly positive Weil-Felix reaction in 30 per cent. of the cases about seven days after the onset. One patient died. The incubation period ranged from 7 to 24 days.

The authors emphasize the risk, not only to the persons inoculated, but also to those who come into contact with them, and stress the favourable results obtained by using a killed ether-extracted yolk-sac vaccine. [Although living vaccines are not likely to be widely used in future, there may be circumstances in which their use is justified in spite of the slight risks involved. The brilliant results obtained in French North Africa cannot be ignored.]

John W. D. Megaw.

HAAGEN, E. & CRODEL, B. Versuche mit einem neuen getrockneten Fleckfieberimpfstoff. [**Investigation of a New Dry Vaccine against Typhus Fever.**] *Zent. f. Bakt.* I. Abt. Orig. 1944, July 12 & Dec. 20, v. 151, Nos. 6 & 7, 307–11 ; 369–73, 5 charts.

The authors begin by quoting the barbarous experiments of DING [see this *Bulletin*, 1944, v. 41, 116] as showing that the commonly-used typhus vaccines do not prevent attacks of the disease though they greatly lessen its severity by an antitoxic effect. The experiments described in this paper are somewhat less brutal than those of Ding but it seems unlikely that the human subjects concerned could have been "volunteers". The investigation is said to have been carried out by order of the chiefs of the Air Force Health Services and with the approval of the highest authorities, including Hitler himself.

The vaccines consisted of preparations of yolk-sac cultures of murine and epidemic rickettsiae attenuated by drying *in vacuo* and storage.

Dried murine vaccine after four-weeks' storage was injected intramuscularly into eight persons of whom three had a febrile reaction and an *OX19* titre which ranged from 1–500 to 1–2,000 ; the others had no febrile reaction but their Weil-Felix titres ranged from 1–50 to 1–1,000. The vaccine after storage for 5–6 months seems to have caused no reaction in any of the eight other subjects who were inoculated, but in two of them the Weil-Felix titre was 1–2,000 four weeks later, in one it was 1–200, and in the remaining five it was zero.

A group of 40 persons received the vaccine after it had been stored for eight months ; there were no reactions. A week later these persons received an epidemic-typhus vaccine prepared in the same way, but stored for 14 to 60 days. Within three days half of them were already febrile and by the end of seven days 39 were febrile. Altogether, at some period, 23 had temperatures of 39°C. or over, and 8 had temperatures in excess of 40°C. By the end of 17 days the temperature of 30 of the persons had fallen to normal.

The two charts illustrating the paper show fever curves conforming to types commonly seen in mild typhus fever.

About 16 weeks after the second vaccination a suspension of a virulent culture of *Rickettsia prowazeki* was rubbed into the scarified skin of each 40 persons ; no reaction was observed in any case.

The authors admit that the vaccine is not suitable for general use, but they claim—not without reason—that it is "anti-infectious", and not merely antitoxic. *John W. D. Megaw.*

GROUPE, V., NIGG, Clara & MACFARLANE, J. O. **On Increasing the Yield and Potency of Typhus Vaccine prepared from Infected Yolk Sacs.** *J. Immunology.* 1946, Aug., v. 54, No. 4, 303–14. [14 refs.]

This paper was received for publication on June 23, 1944, but was withheld for some time "for reasons of national security."

The authors describe methods of increasing the yield and potency of epidemic-typhus vaccines, prepared by Craigie's method from yolk sacs infected by Cox's method.

The potency of the vaccine was tested (1) by the mouse-protection test ; in which the power of sera of guineapigs immunized by the vaccine to neutralize lethal doses of the rickettsial toxins was used as the standard ; mice being used as the test animals ; (2) by complement-fixation tests ; and (3) by estimating the number of rickettsiae in strained smears of the vaccine.

The total yield for each inoculated egg was increased : (1) by incubating the eggs in the vertical position with the air-sac end uppermost ; (2) by delaying the death of the embryo through the use of suitable doses of the inoculum ; (3) by harvesting only the embryos still alive on the day on which the peak of embryo deaths occurred ; and (4) by inoculating the eggs on the 7th instead of the 6th day of incubation.

The potency of the vaccine was highest when the yolk sacs harvested were from embryos dying on the day of peak of deaths of the embryos, or on the previous day, and from those still living on the day of peak of deaths.

Taking into account the three factors—yield, potency, and cost of candling, the best results were obtained when the peak of embryo deaths fell on the 7th day after inoculation, all embryos dying before the 6th day being discarded. When the peak of deaths fell on the 6th or 8th day the yolk sacs still living on those days could profitably be harvested, but dead embryos should be discarded.

John W. D. Megaw.

Cox, G. W. **Lavaca County Typhus Research Unit Narrative and Progress Report for the Period October 1st, 1944, to December 1st, 1945.** *Bull. Office Internat. d'Hyg. Publique.* 1946, Apr.–May–June, v. 38, Nos. 4, 5 & 6, 235–50.

This is an interim report of an investigation into murine typhus in a heavily infected county in Texas. No less than ten teams of experts are engaged in the study of the various aspects of the disease.

In view of the expected appearance at a later date of a complete report this abstract will deal only with a few points of interest.

Evidence has been obtained which suggests that control measures, especially the use of vaccine, may have caused a reduction in the incidence of the disease in the county; in 1944 there were 157 cases and in 1945 only 51. Dusting of the rat runs with DDT caused at least a temporary reduction in the rat-flea incidence, and this may be important because there was a direct association between this incidence and the prevalence of the disease.

In urban areas the great majority of the rats gave positive complement-fixation reactions; in rural areas nearly 50 per cent. of the rats reacted. Three species of fleas were found infected—*Xenopsylla cheopis*, *Leptopsylla segnis*, and *Echidnophaga gallinacea*. A few pools of lice found on rats were infected; all the mite pools were free from infection.

Encouraging results were obtained from the use of sodium fluoroacetate as a poison for rats and mice.

The brown rat, *Rattus norvegicus*, was found only in an urban area; the roof rat, *Rattus rattus*, was found throughout the county.

The arthropods found on rats were :—6 species of fleas, 4 of mites, and 2 of lice.

Among 92 cats, 19 per cent. were serologically positive, and among 112 dogs 79 per cent. were positive. On the other hand among 49 large pools of fleas from cats and dogs only 3 gave evidence of infection, and even this finding is said to "require checking."

The significance of the complement-fixation test is said to be doubtful. Serological tests suggest the possibility that cotton rats, wood rats, bats and squirrels may harbour infection, but few fleas were found on any of the wild animals examined in the area. *John W. D. Megaw.*

Pomales Lebron, A., Arbona, G., Morales Otero, P. & Koppisch, E. **The Complement-Fixation and Weil-Felix Reactions in a Study of Typhus among Wild Rats.** *Puerto Rico J. Pub. Health & Trop. Med.* 1946, June, v. 21, No. 4, 350–56. [Spanish version 357–63.]

Serological tests were carried out between December 7, 1944, and June 22, 1945, on 443 rats caught in San Juan and Santurce, Porto Rico. More than 500 cases of murine typhus had been reported from these localities during the previous five years. In the complement-fixation tests an epidemic type of antigen was used because no murine antigen was available.

Of the 443 sera 30 were anticomplementary; among the remaining rats 54 per cent. gave positive reactions. Among the 24 small (young) rats 42 per cent. were positive, and among the largest (oldest) 70 per cent. were positive.

No significant difference was observed in the percentage of positives among the three species of rats, *Rattus norvegicus*, *R. rattus*, and *R. alexandrinus*, or among rats caught at seasons of high and low incidence of the disease.

The Weil-Felix test was carried out on 251 rats; 61 of these gave positive reactions, whereas 139 gave positive complement-fixation reactions.

Among 112 rats that gave negative complement-fixation reactions, 17 per cent. were positive with the Weil-Felix test.

The author suggests that young rats should be chosen, as far as possible, for the tests, and he points out that positive complement-fixation reactions do not necessarily mean that a transmissible infection is present in the animals.

John W. D. Megaw.

DIAZ-RIVERA, R. S., SANTOS, J. J. & PEREZ-SANTIAGO, E. **The Treatment of Murine Typhus with Para-Aminobenzoic Acid. A Preliminary Report.** *Bol. Asoc. Med. de Puerto Rico.* 1946, June, v. 38, No. 6, 189–94, 3 charts.

The authors report decided benefit from the administration of *para*-aminobenzoic acid to three patients suffering from murine typhus. There were no controls. Daily doses of 16–24 gm. were given: the treatment was started on the 5th, 7th and 8th day respectively, and in each case clinical improvement was observed within 24 to 48 hours. In two cases, the temperature fell by crisis; all three patients were free from fever or symptoms within three or four days, "and the course of the disease was practically shortened." No toxic symptoms were observed. The total dosage ranged from 86 to 136 gm.

John W. D. Megaw.

KIKUTH, W., with SCHILLING, Ilse. Chemotherapeutische Versuche beim Fleckfieber (*R. mooseri*) mit Methylenblau. [**Investigation of the Chemotherapeutic Action of Methylene Blue in Murine Typhus.**] *Zent. f. Bakt.* I. Abt. Orig. 1944, July 12, v. 151, No. 6, 293–302, 5 figs. [11 refs.]

In a large series of controlled experiments it was found that methylene blue, administered in suitable doses by subcutaneous injection or by the mouth, had a pronounced beneficial effect on mice inoculated with lethal doses of *Rickettsia mooseri* intraperitoneally or by the nasal route.

Combined treatment with immune serum and methylene blue did not give better results than were obtained by the dye alone.

The criterion adopted in the tests was the survival of the animals for longer than ten days, but some of the animals surviving for that period died later, presumably, according to the author, because of generalization of the infection or of anaemia caused by methylene blue.

The possibility of using the drug in human patients is discussed in guarded terms; early and continued treatment with therapeutic doses by the mouth is considered worthy of a trial.

John W. D. Megaw.

WILEY, J. S. **Recent Developments in Murine Typhus Fever Control.** *Amer. J. Pub. Health.* 1946, Sept., v. 36, No. 9, 974–83, 4 figs.

In 1944 the reported cases of murine, "or rat-borne", typhus in the U.S.A. numbered 5,300, and in 1945 the figure was 5,167. The author believes that many cases are not reported and that the true figures may be five times as great.

A map shows the geographical distribution of the disease in the U.S.A.; it appears that north of about 33°N. the disease is almost entirely restricted to small areas in the business sections of towns and cities, but that south of this latitude many cases occur also in residential and rural areas.

Some of the new methods of control described by the author are as follows: Flea control by a powder containing 10 per cent. of DDT is said to give quick though temporary results. The powder is applied in localized patches by a hand shaker to rat runs and other places frequented by rats; the amount needed for each establishment varies from one to five pounds. This method is now used as a routine a few days before the employment of any method of rat

control. Calcium cyanide is preferred for dusting rat burrows because it kills the rats as well as the fleas.

A new method of poisoning rats is said to be more than ten times as efficient as any of those formerly used. The poison is "1080" (sodium fluoroacetate); 12–14 gm. dissolved in one gallon of water is distributed in paper cups of the ¾ oz. size. It is stated that during a period of two months an average of six rats to ten cups was the rate of killing in 67 rat-proofed establishments. The poison has the disadvantage of being very deadly to dogs and cats. Red squill is still largely used when there is risk to other animals.

Mention is made of "ANTU" (alpha naphthyl-thiourea) which is used as a 20 per cent. dusting powder in the same way as DDT, but with the object of killing the rats, which ingest the poison when they lick the part of the body that has come into contact with the powder. This method is effective against Norwegian rats, but not against most other species, and tolerance is quickly established.

The original paper can be read with profit by all who are concerned with the control of rats and their fleas. *John W. D. Megaw.*

JOHNSON, D. H. **The Rat Population of a newly established Military Base in the Solomon Islands.** *U.S. Nav. Med. Bull.* 1946, Oct., v. 46, No. 10, 1628–32.

This military base was a beach-head at Cape Torokina on Bougainville Island with a sparse Melanesian population living in small villages along the shore. Three species of rats inhabited, or came to inhabit the area, of which one was the domestic rat, *Rattus rattus*, which was introduced from the ships of invasion. The other two, native rats, were *Rattus exulans*, closely related to the *R. concolor* group, and *Rattus praetor* which is related to the *R. leucopus* or *R. ringens* rats. *Rattus exulans* was the domestic or commensal rat of the locality, readily adapting itself to camp life, provided with an excellent food supply, and because of its small size (225 mm. total length) able to gain entrance with exceptional ease into the furniture and furnishings of the camp. This rat can dig burrows and climb, but has a lower reproductive rate than *R. rattus*. *Rattus praetor* is a large, heavy-bodied rat with the proportions of *R. norvegicus*, is restricted to the Solomon Islands and Bismarck archipelago, and is a strictly sylvatic rodent. "There is strong circumstantial evidence that *R. praetor* played a part in the epidemiology of tsutsugamushi diseases or scrub typhus . . . at the Juba River outpost." They were infested with the chiggers of trombiculine mites. *W. F. Harvey.*

RIPLEY, H. S. **Neuropsychiatric Observations on Tsutsugamushi Fever (Scrub Typhus).** *Arch. Neurology & Psychiatry.* 1946, July, v. 56, No. 1, 42–54. [10 refs.]

"Neuropsychiatric observations were made on a group of 51 patients with tsutsugamushi fever during an outbreak on Goodenough Island. Mortality was 25 per cent. All patients exhibited involvement of the central nervous system, manifestations ranging widely from transient toxic cerebral symptoms to evidence of severe, widespread inflammation, resulting in coma and death. Pathologic changes in the central nervous system were similar to those found in other organs of the body and consisted of focal lesions characterized by necrosis, thrombosis and perivascular infiltration with numerous mononuclear cells, lymphocytes and plasma cells and rare polymorphonuclear leukocytes. The rate and degree of recovery varied considerably. Twenty-nine per cent. of patients on whom follow-up data were available, eighteen months after the acute phase of the disease, showed residual manifestations, most of which

appeared to be secondary to organic changes of the central nervous system. None had symptoms of sufficient severity to prevent performance of useful work. During the acute illness symptomatic treatment and good nursing care were of major importance. During convalescence graduated activity under medical supervision and prompt treatment of psychoneurotic manifestations facilitated recovery. Psychotherapy, with a brief analysis of personality reactions, explanation, reassurance and encouragement, was found to be of benefit."

DE PAULA, A. Tifo exantemático em Juiz de Fóra. Dois sintomas novos constantes nos casos observados. [**Exanthematic Typhus in Juiz de Fora (Minas Gerais). Two New Signs constantly observed in our Cases.**] *Rev. Brasileira Med.* Rio de Janeiro. 1945, Nov., v. 2, No. 11, 907–11. English summary.

All the five patients in whom the new signs were seen lived in the same house; four were attacked within a period of 12 days in June 1945; the fifth fell ill in August 1945. The last patient had been bitten by ticks three days before the onset, there was no history of bites by arthropods in any of the other cases. None of the patients died, and only one had a severe attack.

The Weil-Felix responses were of the *OX19* type, but most of the tests were carried out some weeks after recovery. The *OX19* titre in the last case, in which the test was made during the illness, rose to 1–1,210 and there was a positive reaction 1–640 with the *OXL* strain isolated by de Magalhães.

The signs are described as (1) straw-coloured vesicles situated on the palate and anterior pillars of the fauces, and (2) white porcelain-like ulcers with irregular margins on each side of the anterior pillars of the fauces.

A tick-infested dog was suspected of being the source of infection, but the authors state that in Brazilian typhus the possibility of transmission by bugs, lice and fleas, as well as by ticks, must be considered. *John W. D. Megaw.*

PLOTZ, H. **The Interpretation of the Weil-Felix Agglutination Test in Rocky Mountain Spotted Fever.** *J. Lab. & Clin. Med.* 1946, Sept., v. 31, No. 9, 982–6. [18 refs.]

In 19 cases of Rocky Mountain spotted fever in which the diagnosis was confirmed by the complement-fixation test or by isolation of the infecting agent, the author carried out Weil-Felix tests on two to four occasions with controlled non-motile strains of *Proteus OX19*, *Pr. OX2* and *Pr. OXK*. The technique employed was that described in *Diagnostic Procedures and Technique* (American Public Health Association, 1945).

The following analysis shows the four types of reaction observed :—

Analysis of Reactions

Cases	*OX19* Titre	*Range*	*OX2* Titre	Range
11	Higher than *OX2*	160–2,560	Lower than *OX19*	0–640
4	Lower than *OX2*	0–160	Higher than *OX19*	640–2,560
3	Low or negative	0–40	Negative	
1	Same as *OX2*	320	Same as *OX19*	320

The author states that these results are comparable with those obtained by SPENCER and MAXCY (*Pub. Health Rep.*, 1930, v. 45, 440) and DAVIS and PARKER (*ibid.*, 1932, v. 47, 1511); they show that the commonest type

of reaction is a high-titre agglutination of *Proteus OX19*, but they differ from the typical reaction shown for the disease in the table prepared by FELIX in 1933, in which the average reaction with *OX19*, *OX2*, and *OXK* is shown as +, whereas the *OX19* average titre in louse-borne and flea-borne typhus is shown as +++. [For a later table prepared by Felix see this *Bulletin*, 1943, v. 40, 231, in which the tick borne typhus fevers are shown as belonging to the "undetermined immunological sub-group" and the louse-borne and flea-borne typhus fevers of South Africa are included in the same sub-group.]

The author suggests that the usual types of reaction are as shown in the following table :—

	OX19	*OX2*	*OXK*
Epidemic and murine typhus ...	++++	+	0
Scrub typhus	0	0	++++
Rocky Mountain spotted fever (*a*) ...	++++	+	0
(*b*) ...	+	++++	0

It appears that the usual type of reaction in Rocky Mountain spotted fever is of the *OX19* type and that when the *OX2* titre is 1–320 or over the disease can be suspected. The author states that "since the Weil-Felix proteus agglutination is considered a non-specific test the final laboratory diagnosis will depend upon the isolation of the infectious agent or the demonstration of specific antibodies."

[A study of the detailed table showing the reactions suggests that the types of response obtained in Rocky Mountain spotted fever would be more accurately indicated as follows :—

OX19 titre	*OX2* titre	*OXK* titre
0 to ++++	0 to ++++	0

Another point that emerges from the table is that the complement-fixation reaction in five cases became positive later than the Weil-Felix, for example, an *OX2* titre of 1–1,280 is shown in one case on the 21st day when the fixation reaction was still negative, and in another on the 20th day there was an *OX19* titre of 1–1,280 with a fixation reaction still negative. In these cases the fixation test was found positive on the 40th and 140th days, respectively. On the other hand, in three cases the fixation test was positive earlier than the Weil-Felix ; in one case it became positive on the 4th day, and in another on the 7th day, whereas the Weil-Felix reaction did not become positive till later, in fact in the former case it was still negative on the 23rd day, the last on which the test was carried out.] *John W. D. Megaw.*

ANDREW, R., BONNIN, J. M. & WILLIAMS, S. **Tick Typhus in North Queensland.** *Med. J. Australia.* 1946, Aug. 24, v. 2, No. 8, 253–8, 2 figs. [10 refs.]

The authors state that up to 1944 it was generally believed that tick-borne typhus did not occur in Australia. In this and the two following papers, a detailed description is given of the clinical and experimental features of a disease to which the authors provisionally give the name North Queensland tick typhus.

Twelve cases were seen between March 1944 and February 1945 in the Atherton plateau which is at an altitude of 2,000 to 2,500 feet. The climate of the plateau is relatively temperate, and the rainfall is about 60 inches.

Scrub typhus had occurred in certain parts of the area among the many thousands of troops engaged in military exercises in the belts of " rain forest ", of which many occur in the plateau.

Only one species of tick, *Ixodes holocyclus*, was found on human hosts in the area, but three other man-biting ticks were known to occur: *Haemaphysalis bancrofti*, *Boophilus annulatus microplus*, and *Rhipicephalus sanguineus*. Seven of the patients were known to have been bitten by ticks; in one case the tick, *I. holocyclus*, was still attached to the patient at the time of admission to hospital. In the cases in which there was no history of tick bite the patients had been exposed to special risk of bites.

An eschar with associated lymphadenitis occurred in nine cases, and in two of these an adult tick had been found at the site of the lesion.

Ten of the 12 cases occurred in August and September, the period of the early spring rains, when *I. holocyclus* was most abundant.

The clinical features as described conform to those of a mild fever of the typhus group; the average duration was 7½ days, with an extreme range of 2 to 12 days. A rash was seen in 11 cases; it was very variable in appearance, macular, papular, or maculo-papular.

The maximum Weil-Felix titres were as follows:—In 9 cases the *OX19* titre was 1–320 or over; in 3 of these the *OX2* titre was 1–160 or over, but in each case it was lower than the *OX19* titre; in one case there was a rising-titre *OX19* reaction with a maximum of 1–160; in the remaining 2 cases the *OX2* titres were higher than the *OX19*, being 1–320 and 1–640, whereas the *OX19* titres were 1–80 and 1–160.

The *OXK* titre never exceeded 1–80 and it was not of the rising-titre type. [There is a general correspondence between these findings and those reported by Plotz in cases of Rocky Mountain spotted fever (see Plotz above).]

Rickettsial strains were isolated from two patients by intraperitoneal inoculation of 1·0 cc. of fresh blood into vitamin-deficient white mice, which reacted with enlargement of the spleen and a peritoneal exudate containing rickettsia-like bodies. Guineapigs inoculated with spleen suspensions of the mice reacted with fever and scrotal reaction, but recovered. Several successive passages were made through guineapigs.

Several other cases were seen which might have been of the same kind, but the diagnosis remained doubtful.

Samples of serum from five of the patients, and from two murine-typhus patients infected in the same area, were sent to Col. Harry Plotz who found that none of the tick-typhus sera gave positive rickettsia-agglutination reactions when tested against epidemic and murine rickettsiae, except for one reaction (1–80) against epidemic rickettsiae; the murine-typhus sera reacted at titres of 1–5,120 and 10,240 with murine rickettsiae and at titres of 1–320 and 1,280 with epidemic rickettsiae.

Complement-fixation tests of all the sera were carried out with antigens of the following types:—epidemic typhus, murine typhus, boutonneuse fever, South African tick-bite fever, and Rocky Mountain spotted fever. The two murine-typhus sera reacted with murine antigens at titres of 1–60 and 1–80, otherwise all the reactions were completely negative so that the tests did not indicate any immunological relationship between the North-Queensland tick typhus and any of the above fevers of the typhus group.

John W. D. Megaw.

PLOTZ, H., SMADEL, J. E., BENNETT, B. L., REAGAN, R. L. & SNYDER, M. J. **North Queensland Tick Typhus : Studies of the Aetiological Agent and its relation to other Rickettsial Diseases.** *Med. J. Australia.* 1946, Aug. 24, v. 2, No. 8, 263–8. [23 refs.]

The serological tests carried out by the senior author in connexion with North Queensland tick typhus have already been mentioned in the abstract above (ANDREW *et al.*). The present paper deals with a further laboratory investigation of a tick-typhus strain of rickettsiae received from Australia in the form of lyophilized yolk-sac material.

Passage of the strain through guineapigs was maintained by intraperitoneal injections of tunica-vaginalis exudate. The strain grew better in tissue culture than in yolk sacs, and the antigen used in complement-fixation tests was prepared from tissue cultures by a method described in the paper.

Sera of guineapigs convalescent from experimentally-induced attacks gave complement-fixation titres ranging from 1–40 to 1–320 when the homologous antigen was used ; negative reactions were observed in these animals when the following antigens were used :—epidemic typhus, murine typhus, Rocky Mountain spotted fever, South African tick bite fever, boutonneuse fever, and Q fever.

On the other hand, guineapigs convalescent from North Queensland tick typhus were found to have a pronounced degree of partial immunity against infection with rickettsiae of South African tick bite fever and murine typhus, but the authors suggest that the immunity may have been non-specific because it was found to have disappeared in the case of two guineapigs tested eight months later, whereas two guineapigs immunized by the North Queensland tick typhus were still fully immune at the end of that time.

The authors emphasize the importance of taking this time factor into account in estimating the significance of cross-immunity tests.

An anomalous result was that sera of North Queensland tick typhus patients gave negative complement-fixation reactions when tested against the homologous antigen : but it is suggested that the sera may have become deteriorated during the long journey from Australia, and the authors accept the findings of the Australian workers in this connexion.

The conclusion reached was that the rickettsia of North Queensland tick typhus differs from the others mentioned above and may well be a hitherto undescribed species. *John W. D. Megaw.*

FUNDER, J. F. & JACKSON, A. V. **North Queensland Tick Typhus : a Comparative Study of the Rickettsia with that of Murine Typhus.** *Med. J. Australia.* 1946, Aug. 24, v. 2, No. 8, 258–63, 1 fig.

The two strains of tick-typhus rickettsiae and the two of murine-typhus rickettsiae mentioned in the preceding paper were closely studied in the laboratory. The tick-typhus strains were cultivated in yolk sacs of embryo chicks, and one of them was maintained through 119 serial passages. Death of the embryos occurred most frequently on the 4th day in eggs kept at 37°C. In the earlier passages rickettsiae were usually scanty, but they became more numerous in the later passages. The murine strains yielded more numerous rickettsiae and the embryo deaths were rather later on the average. Both strains when inoculated intraperitoneally into guineapigs caused very similar febrile and scrotal reactions.

Guineapigs convalescent from attacks caused by each strain showed a considerable, but incomplete, degree of immunity against inoculation by the other strain.

The murine strains could be recovered from the brain of white rats up to 258 days, the tick-typhus strains were non-persistent.

In tissue cultures the tick-typhus strains were found in the nuclei as well as in the cytoplasm of the invaded cells.

Complement-fixation tests were carried out on sera from patients suffering from tick typhus and murine typhus ; the antigens were prepared from yolk-sac cultures ; low-titre reactions were obtained with the homologous antigens and negative reactions with the heterologous.

The reactions of tick-typhus patients were at titres ranging from partial 1–4 to complete 1–32.

Full details are given of the technical methods employed in the study.

John W. D. Megaw.

DENGUE AND ALLIED FEVERS.

SOUBIGOU, X. Une épidémie de dengue à la Martinique. [**A Dengue Epidemic in Martinique.**] *Bull. Soc. Path. Exot.* 1946, v. 39, Nos. 7/8, 270–72.

HUGHES, A. C. C. **The Leucocyte Count in Dengue.** *J. Roy. Nav. Med. Serv.* 1946, July, v. 32, No. 3, 194–6.

The author refers to a statement in the *Roy. Nav. Med. Bull.*, No. 13, 20, to the effect that in dengue a shift to the left in the neutrophiles does not occur. The statement precedes an abstract from a paper by SABIN *et al.* [this *Bulletin*, 1944, v. 41, 1031] which describes the invariable shift to the left encountered in sandfly fever. Reference is also made to the work of SIMMONS *et al.* [this *Bulletin*, 1931, v. 28, 613] which reported an invariable left shift in dengue after the first day of illness. This feature, together with leucopenia, Simmons regarded as " the most reliable single diagnostic sign of dengue ".

The present author rightly points out that if there is in fact such a difference in the behaviour of the neutrophiles in dengue and sandfly fever, it would be of important diagnostic value and would indeed throw doubt on the accepted close aetiological resemblance between the two diseases : and with these conflicting statements in mind, he carried out serial blood counts on the staff of a hospital ship in the Indian Ocean, who had probably acquired dengue in Calcutta. Adequate epidemiological and clinical evidence is given in support of his diagnosis.

Schilling and Cooke-Arneth counts were carried out sixty times on different days of the illness. From the 3rd to the 6th day there was a fall in the total count, which commonly became normal before the 11th. At some stage, the total leucocytes usually fell to below 5,000 per cmm. and counts of less than 3,000 were not uncommon. The lymphocyte count was low by the 2nd or 3rd day, though it never fell below 1,000.

There were no significant changes in the monocytes or eosinophiles ; but the neutrophiles fell in every case after the 2nd day, usually to 2,000 or less at some stage. Segmented leucocytes usually fell below 1,000 on the 2nd or 3rd day. Stab cells invariably increased on the 2nd day, and remained high in proportion to the segmented cells for the first five days : the juvenile cells were increased initially, but to a less extent and constancy.

A left shift in the Cooke-Arneth count occurred and was at its maximum between the 2nd and 5th days.

The return of the neutrophiles to normal was slow, and often was incomplete on the tenth day : during convalescence, Turck cells were frequent.

Detailed counts of six patients are shown in a table. The author's results correspond with those of Simmons in experimental dengue, and do not differ essentially from those of Sabin in sandfly fever: he therefore concludes that the leucocyte count is not likely to assist in the differential diagnosis of these two diseases. *H. J. O'D. Burke-Gaffney.*

LIVESAY, H. R., WILSON, D. J., POLLARD, M. & WOODLAND, J. C. **Experimental Studies of Bullis Fever and Dengue Fever.** *Amer. J. Trop. Med.* 1946, July, v. 26, No. 4, 379–81, 1 chart.

Three healthy volunteers were inoculated with material regarded as containing the infective agent of Bullis fever; in two cases a yolk-sac culture originating from a tick was used; in the third 2 cc. of whole blood from a patient was given; in all the cases the subcutaneous route was employed.

On the 4th day all the volunteers reacted with malaise, leucopenia, headache, lymphadenopathy, and mild fever. [From the charts it appears that the fever lasted about five days and showed a tendency to be biphasic. The temperature never exceeded 99·5°F.]

The volunteers were inoculated, 27 days after defervescence, with 0·4 cc. of dengue-infected human serum. All three, and also a normal-control volunteer similarly inoculated, developed a "typical syndrome of dengue fever" on the 6th or 7th day; the fever lasted six to seven days and was accompanied by malaise, headache, leucopenia, and a generalized rash. The maximum temperatures ranged from 102·4 to 104·5°F.

The authors state that on the basis of this challenge experiment, no relationship between Bullis fever and dengue could be demonstrated, though they add that it is possible that strain variations may alter the results to some extent.

In their reference to the aetiology of Bullis fever the authors remark that "the Bullis fever agent has been described as rickettsia-like in morphology." This statement seems to suggest that they maintain an open mind regarding the nature of the causal agent. *John W. D. Megaw.*

WEBER, F. C., OPPEL, T. W. & RAYMOND, R. W. **A Mild Exanthematous Disease seen in the Schouten Islands.** *Amer. J. Trop. Med.* 1946, July, v. 26, No. 4, 489–95. [11 refs.]

During 1944 and 1945, the authors studied 48 cases of a mild fever lasting one to seven days and accompanied by an exanthem which persisted for seven to ten days; the patients had pain and swelling of the joints, enlargement of the lymph nodes and leucopenia. Medical men at three hospitals in the Schouten Islands, north of New Guinea, independently regarded the condition as distinct and unusual, and gave it various names.

Of the cases seen by the authors, 31 were treated at one hospital in the months of December 1944, and April, May, June and July 1945. At another hospital 17 cases were seen in March and April 1945; eight of these patients were members of the hospital staff, who were admitted between March 20 and April 1.

The percentage incidence of some of the chief features was as follows:—maculo-papular rash, 100; enlargement of lymph nodes, 80; temperature 100°F. or over, 75; headache, 50; swelling of ears, 46; swelling of skin over elbows and knees, 46; swelling of hands and feet, 25; joint involvement, 31; effusion into a joint, 10. The total leucocyte count was less than 4,000 in 39 per cent. of the cases. The rash appeared within the first three days in 85 per cent.; at first it was a macular erythema occurring on the front and sides of the chest, it spread over the trunk and limbs, sometimes extending

to the face ; the palms and soles were affected in 25 per cent. of the cases. The macules were about 10 mm. in diameter and commonly a papule appeared in the centre of each.

The duration of the fever was :—one or two days in 15 cases ; three days in 17 ; four to six days in 14 ; and seven days in 1. Convalescence was always rapid.

Cultures of the blood, urine, and stools gave no information bearing on the aetiology. Agglutination tests for scrub typhus, the enteric group, and brucellosis were negative.

The disease differed from dengue in the more gradual onset, the mildness of the attacks, the absence of saddle-back fever curves, the slight degree of pain, the more marked stiffness and swelling of the joints, and the more papular type of the rash, which also appeared earlier and lasted longer. The authors state that " only 10 typical cases of dengue were observed during the time these cases were being seen."

Although the disease resembled the " polyarthritis " described in Australia by HALLIDAY and HORAN [this *Bulletin*, 1944, v. 41, 279] it was regarded as differing, in being associated with leucopenia, in the less severe involvement of the joints, and the more pronounced rash.

In a foot-note it is stated that an epidemic is reported to have occurred in Bougainville, of a fever " almost exactly the same " as the one described by Halliday and Horan.

The authors make no claim that " the clinical evidence is sufficient to establish this disease as a new entity," and they state that the comments by the reviewer on the paper by Halliday and Horan apply equally to the present outbreak.

John W. D. Megaw.

PLAGUE.

ROUX, A. H. & MERCIER, C. Sur cinq cas de peste pulmonaire primitive dont trois suivis de guérison, observés à l'hopital civil d'Oran. [**Five Cases of Primary Pneumonic Plague with Three Cures.**] *Bull. Soc. Path. Exot.* 1946, v. 39, Nos. 5/6, 173–8.

The first case in this series was that of a man admitted to hospital after the rapid death of four members of a family. He had continuous ineffective cough, high temperature, and blood-stained sputum ; there were no buboes. Plague bacilli had been found in the sputum and were found also *post mortem* in the lung lesion. From this one patient, infection was transmitted to three persons in hospital and in each of these the affection had all the signs of plague bronchopneumonia, without development of buboes. Two patients were women and the third was the hospital chaplain. The fifth was a woman, who was also admitted to hospital and whose husband had been one of the original four patients who had died rapidly from presumed plague. Both of the men died and the three women were cured with dosages totalling 65 to 73 gm. sulphathiazole in 15 to 18 days. Recovery of three cases out of five from primary pneumonic plague is remarkable and the result is attributed entirely to the use of the sulphonamide drug.

W. F. Harvey.

RIEMAN, E. H. **Antu. A Progress Report detailing Results obtained with this New and Highly Effective Rodenticide.** *Soap.* New York. 1946, Oct., v. 22, No. 10, 135–7, 153, 1 fig.

A progress report of results obtained.

CHOLERA.

STOWMAN, K. **Cholera Situation, Summer 1946.** *Epidemiological Information Bull.* (UNRRA Health Division). Washington, D.C. 1946, v. 2, No. 16, 674–8.

It is not surprising to read that epidemiological data on cholera in the Far East are not yet adequate and perhaps not wholly accurate. Recent information is not available from Japan, while in China at least sixteen provinces are affected. Serious consequences may attend the appearance of epidemic cholera in the four provinces of Southern Manchuria. At present Shanghai, where cholera reporting and serious measures of treatment and prevention are practised, seems to be the chief centre of cholera in China. Tonking in Indo-China provides no information, but there have been outbreaks in Cochin China and in Cambodia. The cholera outbreak in Siam is in its third year. Malaya and Burma do not seem to have been unduly affected, but parts of India have had a specially bad cholera year. Cholera in Ceylon has been insignificant and "there has been no case of cholera west of India since 1931, apart from the Afghanistan Iran outbreak of 1938-39." *W. F. Harvey.*

SEAL, S. C. **A Note on Cholera Outbreaks (1944–45) in the Singur Health Centre Area, Bengal, with special reference to Control Measures.** *Indian Med. Gaz.* 1946, Aug., v. 81, No. 8, 321–6, 1 map & 1 chart.

Note may well be taken of the idea to set apart a special area for investigation into the numberless problems which confront the epidemiologist with regard to outbreaks of a specific disease. The area in question, rural, 33 square miles with a population of 63,000, has had 27 outbreaks of cholera within a year studied by the All-India Institute of Hygiene and Public Health. One important objective was to find a "simpler but efficient method of control within the means of the local health organization and the community." In summarizing the article it seems best, and most useful, to confine oneself to an abbreviated version of the detailed instructions given "before leaving the patient's house":—(1) Administer sulphaguanidine according to instructions. (2) Give enough fluid to the patient; cocoanut, alkaline or glucose water. (3) Keep the patient warm. (4) Call the doctor if the patient takes a bad turn. (5) Keep bleaching powder solution (1 teaspoonful/gallon) in an earthen vessel for the hands of attendants and for disinfection at all times. (6) Collect vomit and stool in earthen pans; disinfect with bleaching powder, and bury them in a pit. (7) Disinfect pans to be re-used with strong bleaching powder solution. (8) Keep medicine, utensils and other materials used by the patient strictly separate; to be finally buried or disinfected. (9) Bury the food left by the patient and burn, bury, or disinfect bedding, (10) Never wash anything in contact with a patient in a tank or other water source. (11) Wash your own hands after all occasions of contact with the patient and keep away from the kitchen. (12) Keep children and non-attendant adults away from the patient. (13) Use only running water for household purposes and boil all drinking water for the duration of the outbreak. (14) Cover all foods; eat them all hot, if practicable, and drink only boiled milk. Disinfect the hands always before eating or drinking. (15) Avoid irritant food and food from unknown sources. (16) Take acid mixture (Acid sulph. aromat. 3; Spt. chlorof. 1), if a contact; 20 min. in an ounce of water, twice daily. Take a dose of sulphaguanidine and notify the doctor if suspicious symptoms appear. (17) Treat all excreta in the subject of suspicious symptoms in the same way as those of an actual patient. (18) Ask friends and relatives to keep away from the house. *W. F. Harvey.*

SEN, S. N. **Studies on the Biochemistry of the "Cholera-Red" Reaction. Part I.** *Indian J. Med. Res.* 1946, May, v. 34, No. 1, 151–5.

Biochemical study of the metabolic activities of bacteria has provided not only interesting facts regarding the life of those lowly unicellular organisms, but at the same time furnished tests for the differentiation of species. Bacteria produce de-amination or decarboxylation of the nutrient amino-acids. The "cholera-red" reaction "is due to the presence of a nitroso derivative either of indole or of a compound containing indole ring derived from tryptophan and nitrate." Its absence is an important negative test in cultures containing no inhibitory glucose, although other vibrios also may give a positive reaction. Experiments are detailed in this article, which show that reducing agents such as "glucose, cysteine and ferrocyanide exert an inhibitory influence on the 'cholera-red' reaction" and that they act either by inhibiting the formation of the enzyme concerned or by diverting the course of enzymic reaction so that the particular end product to which positive reaction is due is not formed. As might be expected, on this view, oxidizing agents promote the reaction, acting as "catalysts". *W. F. Harvey.*

SEN, S. N., BASU, P. N. & CHAKRABORTY, D. C. **Studies on the Biochemistry of the "Cholera-red" Reaction. Part II.** *Indian J. Med. Res.* 1946, May, v. 34, No. 1, 157–60.

In this continuation of studies, investigation was made into the nature of the enzymatic reaction involved. A cell enzyme may only be identifiable by its specific activity, especially when, as seems to be the case with the cholera vibrio, it is not to any extent separable from the cell. Washing of the vibrios of a culture which had failed to give the reaction resulted in its becoming strongly positive. "As the positive reaction was obtained within the resting phase of the cells it appears that the initial negative reaction with whole culture was due to non-formation of the end product, though the enzyme was present." The enzyme action for break-down of tryptophan was prevented by the reducing agent glucose, and its presence was demonstrated after washing away the glucose. A modification of the technique of the reaction is suggested by the authors: a suspension of a 5- to 6-hour ordinary culture of vibrios is added to a sterile solution of tryptophan and sodium nitrate. The addition of sulphuric acid, after 45 to 60 minutes, elicits the "cholera-red" reaction.

W. F. Harvey.

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS.

FLETCHER, J. P., DOUGAN, A. A. & SAMMON, G. K. **Amoebiasis.** *Canadian Med. Ass. J.* 1946, Sept., v. 55, No. 3, 278–83.

ROBINSON, R. A. **Amebiasis.** *Southern Med. J.* 1946, Nov., v. 39, No. 11, 876–80. [23 refs.]

SINGH, G. **Amoebic Abscess of Liver bursting into Pericardial Cavity.** *Indian Med. Gaz.* 1946, Aug., v. 81, No. 8, 299–301, 1 chart & 4 figs. on 1 pl.

LAWRENCE, D. **Diagnosis of Intestinal Amoebiasis.** [Correspondence.] *Brit. Med. J.* 1946, Nov. 9, 708–9.

The author questions the rationale of "provocative emetine" in the diagnosis of amoebic dysentery, referred to by HILL [this *Bulletin*, 1947, v. 44, 87]

and assumes that it is based on a mistaken analogy with " provocative " N.A.B. in the serological diagnosis of latent syphilis. He points out that, unlike the complex serological significance of the latter, " provocative emetine " solely involves the action of this drug on the amoeba, which is to destroy it.

The author draws the obvious distinction between the presence of vegetative amoebae in the faeces or bowel scrapings in the course of acute and subacute amoebic infections, and the presence of cysts in the " quiescent " phase. In the former condition " the *vegetative* amoeba is almost always found " : in the latter, prolonged daily stool examinations may be necessary over very long periods ; and the practical difficulties of this are discussed.

Academically, in the author's opinion, the solution to the problem may be the unsatisfactory, and even dangerous, one of leaving amoebic dysentery undiagnosed until evidence of the parasite is found. The practical solution—also a hazardous one, although acceptable in principle—suggested by the author, is to tell the patient to return *immediately* if diarrhoea recurs, when the amoeba may be found if it is actively causative. He also mentions special stool culture methods and the possibilities of present work on complement-fixation tests.

[Even though the vegetative form of the amoeba " is almost always found " by the experienced observer in the acute and subacute conditions, a number of examinations may be necessary for finding it : regarding the practical difficulties of examining a sufficient number of stool specimens to ensure the detection of cysts in the " quiescent " stage, the reader is referred to the valuable statistical survey by MARSDEN and his collaborator in Australia [this *Bulletin*, 1947, v. 44, 86]. *H. J. O'D. Burke-Gaffney.*

THOMEN, L. F. & READ, H. La reacción de Craig. Reacción de fijación de complemento para el diagnóstico de la amibiasis. [**Craig's Complement Fixation Test in the Diagnosis of Amoebiasis.**] *Bol. Asoc. Med. de Puerto Rico.* 1946, Mar., v. 38, No. 3, 85–94. [37 refs.]

This is a general review of the literature on the subject of Craig's complement fixation tests for *E. histolytica* infections. The methods of carrying out the test and preparation of the various reagents are fully described. The test is considered to be of special value in the diagnosis of amoebic abscess of the liver, lung or other organ, and in the differentiation of amoebic from other forms of colitis in which amoebae cannot be found by direct examination of faecal specimens. *C. M. Wenyon.*

MICHAEL, P. **Intestinal Parasitism. A Statistical Study on 1,000 Patients recently returned from Pacific Area Duty.** *U.S. Nav. Med. Bull.* 1946, Oct., v. 46, No. 10, 1589–96, 5 figs.

Three thousand specimens of stool from 1,000 men recently returned from the Pacific Ocean area were examined for intestinal parasites. The protozoa were identified in iron-haematoxylin-stained smears, and a sucrose flotation technique was used for the determination of helminth infestations.

Two hundred and eighty-nine individuals (28·9 per cent. of the total) were found to harbour protozoal or helminthic intestinal parasites. *Endolimax nana* was the most common parasite (17·6 per cent. being infected), *Entamoeba histolytica* was next in frequency (8·9 per cent.), and others occurred in lesser numbers of men, their incidence being recorded in a table [*Dientamoeba fragilis*, *Trichomonas hominis*, *Chilomastix mesnili*, and the tapeworms do not seem to have been encountered]. The figures for parasitization do not differ materially from those determined for the indigenous population of the United States as a whole. Graphs show the increased frequency of detection of the presence of

parasites on repetition of the stool examinations ; 60 per cent. being discovered on examination of one specimen, and 90 per cent. on that of three specimens [eight specimens were examined at most, and this number (100 per cent. detection) was reached only in examinations for *Entamoeba histolytica* and for *Endolimax nana*].

Of the 89 patients infected with *E. histolytica* 74 were free from gastro-intestinal symptoms ; these 74 had been admitted to hospital for troubles unassociated with the presence of the parasite ; 32·6 per cent. of the 89 harboured small-race *E. histolytica*, 60·7 per cent. large-race, and 6·74 per cent. a combination of both races. None of the patients harbouring the small-race type of parasite suffered from intestinal symptoms. The blood picture of those infected with *E. histolytica* showed no changes attributable to their infestation.

All cases were therapeutically treated : the symptom-free patients with Diodoquin, either alone or in combination with Carbarsone, and the fourteen passing amoebae with emetine. Three negative stools constituted evidence of sterilization after treatment. There is little likelihood of dissemination on a substantial scale of intestinal parasites from those returning from overseas to the indigenous population ; nevertheless, efforts should be made to detect and to eradicate such parasites from service personnel before their release.

A later survey of prisoners of war repatriated from the Far East, based on a single stool examination, showed the incidence of intestinal parasitization, especially with hookworms, to be surprisingly low. *A. R. D. Adams.*

PONTES, J. P. L. Incidência da amebíase e da giardíase no Rio de Janeiro. Estudo baseado no exâme de 165 indivíduos. [**Incidence of Amoebiasis and Giardiasis in Rio de Janeiro.**] *Rev. Brasileira Med.* Rio de Janeiro. 1945, Oct., v. 2, No. 10, 823–35, 2 figs. [84 refs.] English summary.

The author has examined by floatation technique the stools of 165 inhabitants of Rio de Janeiro for evidence of *Entamoeba histolytica* and *Giardia intestinalis* infection. Of the persons examined 62 were patients in hospital while 103 were normal work people. Both parasites were encountered 19 times, giving an infection rate of 11·5 per cent. In no case was dysentery present, though 77 per cent. of those harbouring *E. histolytica* complained of symptoms which might be attributed to the presence of the amoeba. In only 36 per cent. of those infected with *G. intestinalis* was anything abnormal noted. *C. M. Wenyon.*

CHORINE, V. & TANGUY, Y. Influence du régime alimentaire sur le parasitisme intestinal. [**Influence of Diet on Intestinal Parasitism.**] *Bull. Soc. Path. Exot.* 1945, v. 38, Nos. 1/2, 42–6.

For a number of years, both before and during the war, patients submitting themselves for treatment at the Pasteur Institute in Paris have been examined for intestinal protozoal infections. The authors report that the percentage of positive findings recorded increased during the war to double and sometimes three times their pre-war level. This increase is attributed to the change in diet, which became largely vegetarian. It was perhaps to be expected, since it has been shown that in rats the naturally occurring protozoal infections are much reduced when the animals are kept on a diet rich in protein, while these animals are more readily infected with the human Trichomonas when on a diet rich in carbohydrate. *C. M. Wenyon.*

RELAPSING FEVER AND OTHER SPIROCHAETOSES.

INGRAHAM, H. S. & LAPENTA, R. G. **Penicillin in the Treatment of Louse-borne Relapsing Fever.** *U.S. Nav. Med. Bull.* 1946, Nov., v. 46, No. 11, 1719–23.

" 1. Fifty-two patients with Egyptian louse-borne relapsing fever received 1,000,000 units of penicillin each in 25,000 unit doses intramuscularly every 3 hours. A cure of the relapsing fever was obtained in all 52 cases.

" 2. No relapses occurred in the treated group.

" 3. Relapse occurred in 87 percent. of the 53 cases used as controls."

BOURGAIN, M. Sur la conservation du pouvoir infectant des broyats " d'organes réfrigérés ou en putréfaction " de cobayes infectés expérimentalement de récurrente à *Spirochaeta persica* Dschunkowsky 1912. [**The Preservation of the Infective Power of Emulsions of " Frozen or Putrefying Organs " of Guineapigs Experimentally Infected with** *Spirochaeta persica*, **Dschunkowsky 1912.**] *Bull. Soc. Path. Exot.* 1946, v. 39, Nos. 5/6, 185–7.

The author finds that the organs of guineapigs infected with *Spirochaeta persica*, if collected aseptically and preserved in the refrigerator at 0° to 8°C., retain their infectivity for at least 7 days; and cadavers kept at laboratory temperatures, 12° to 18°C., remain infective for 90 hours, without any loss in the virulence of the spirochaetes, even though putrefaction has already taken place.

It is stated that at temperatures of −15° to −20°C. the spirochaetes do not survive for 48 hours, but the experiments are not sufficiently conclusive. [HINDLE's observations (this *Bulletin*, 1934, v. 31, 512) showed that other spirochaetes survive more readily at such temperatures and under these conditions, can even be dried *in vacuo*.]

The author concludes that in the case of *S. persica* the handling of the cadavers of infected animals may be a source of accidental human infections, and that the survival of the spirochaetes in animals after death may be a factor in the maintenance of the infection in nature. *E. Hindle.*

LEES, A. D. **Chloride Regulation and the Function of the Coxal Glands in Ticks.** *Parasitology.* 1946, Aug., v. 37, Nos. 3/4, 172–84, 10 figs. [20 refs.]

The coxal glands are an excretory organ found in Argasid ticks. In *Ornithodorus moubata* and certain other species of the genus these glands come into operation while the tick is still feeding and liberate a profuse watery fluid. [It is through this fluid that the infection of tick-borne relapsing fever takes place, so that the paper is evidently important in relation to the transmission of *Treponema duttoni* from tick to mammal. It remains for the parasitologist to reinvestigate the problems of transmission in the light of the detailed observations on anatomy and physiology set forth in this paper, which is of unusual interest.] The paper can only be briefly reviewed here.

The author shows that *Ornithodorus moubata* takes a blood meal of from two to six times its own weight, and then rapidly excretes through its coxal glands about half the water taken with the meal. The excreted fluid has a much lower concentration of chlorides than is present in the blood or haemolymph of the tick. The author describes the anatomy of the coxal glands and certain organs associated with them. There are a number of small muscles which arise from the body wall and are attached to a bladder-like filtration chamber of the glands. The walls of this chamber are normally folded, but when the muscles contract the chamber becomes enlarged and this, as the author believes, causes a slight pressure difference which is sufficient to cause water to filter from the body spaces of the tick into the cavity of the chamber and so to the exterior. The

paper contains similar studies on *Ixodes ricinus*, in which, owing to the absence of coxal glands, the mechanism for excreting chlorides and a very large bulk of water is entirely different. *P. A. Buxton.*

POSPELOVA-STROM, M. V. & TIBURSKAYA, N. A. [**On the Therapeutic Effect of Penicillin in Tick Spirochaetosis.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1946, v. 15, No. 1, 54–5. [In Russian.]

The authors record the results of penicillin treatment of tick-borne relapsing fever in man and in experimental animals. A laboratory assistant who was infected accidentally with an Iranian strain, was given 33,000 and 50,000 units of American penicillin on the second and third days respectively of the primary attack, with the result that the spirochaetes disappeared during the next three days and were absent for a month. In the course of this period, the patient was treated with osarsol (5 courses of 0·75 gm. daily for 3 days, followed by an interval of 4 days). On the 31st day the patient had a second attack, with a temperature rising to 41·2°C. and up to 18 spirochaetes per field in the blood. After administration of 50,000 units of penicillin on the 32nd day, the temperature dropped, the spirochaetes disappeared after 6 days and never returned again.

The effect of penicillin (of American and Soviet manufacture) was then tested on guineapigs experimentally infected with tick-spirochaetosis. The drug was injected intramuscularly on two successive days in doses of 2, 16 and 20 units per gramme of body-weight, while in the case of the Soviet preparations 1 and 4 cc. were given. Treatment with penicillin not only failed to suppress the attacks or to prevent relapses in guineapigs, but even prolonged the duration of the disease. On the other hand, while there were no deaths among the treated animals the mortality among the controls amounted to 50 per cent.

C. A. Hoare.

LEPROSY.

HANKS, J. H. **A Note on the Numbers of Leprosy Bacilli which may occur in Leprous Nodules.** *Internat. J. Leprosy.* Cleveland, Ohio. 1945, Dec., v. 13, 25–6.

CHAUDHURI, A. K. R. **A Short Note on Heredity in Leprosy.** *Calcutta Med. J.* 1946, July, v. 43, No. 7, 237–8. [15 refs.]

MAFFRAND, R. Lepra ocular. [**Ocular Leprosy.**] *Día Médico.* 1946, Aug. 5, v. 18, No. 32, 1058.

This brief paper speaks of leprous affections of the eye in somewhat general terms, not going into detail nor giving any figures of prevalence of the ocular complications of leprosy. In the tuberculoid form the globe itself does not suffer. Cases which are recorded as leprous iritis and irido-cyclitis, the author states, are not truly leprous but tuberculous, syphilitic or due to sepsis. The lepromatous form does, however, affect the globe and that frequently, particularly the anterior parts, with infiltration of the cornea, especially the upper layers, and later the iris and the ciliary body. The conjunctiva, in spite of the fact that the secretion may contain many lepra bacilli, is not usually itself involved. The sclerotic is affected in a manner similar to the cornea.

Little is said concerning treatment, merely that there is no specific treatment of much avail and that the "results are problematical." Surgical measures may be tried "according to the special circumstances of each case."

H. Harold Scott.

STEIN, A. A. & DOROFEJEW, W. N. Zur Frage der Klinik und pathologischen Anatomie leprösser Iritis. [**Clinical and Pathological Anatomy of Leprotic Iritis.**] *Internat. J. Leprosy.* Cleveland, Ohio. 1945, Dec., v. 13, 43–66, 5 figs. on 1 pl.

BIMBAD, S. M. **Clinical Study of the Blood Glutathione in Leprosy.** *Internat. J. Leprosy.* Cleveland, Ohio. 1945, Dec., v. 13, 31–42.

"1. A study of the glutathione content of the blood in leprosy is of aid in determining the state of the oxidation-reduction processes in the patient.

"2. In the tuberculoid and maculo-neural forms of the disease the total amount of glutathione in the blood does not differ from normal, but the amount of the oxidized form decreases with a corresponding increase of the reduced form.

"3. The qualitative and quantitative values of blood glutathione in patients with lepromatous leprosy of slight and moderate degrees of advancement of the disease and in a regressive stage do not differ from normal.

"4. In the active cases of the lepromatous type of leprosy in which the disease is progressing either rapidly or slowly all of the glutathione values are decreased.

"5. In the reactive phase of leprosy there is a marked decrease of reduced glutathione and the total value though the amount of the oxidized form tends to remain within normal limits.

"6. Determination of the blood glutathione values in leprosy is of value in ascertaining the extent of compensation of the leprosy process."

FIGUEREDO, N. & DESAI, S. D. **Trial of Penicillin in a Case of Leprosy.** *Leprosy in India.* 1946, Apr., v. 18, No. 2, 53.

"A lepromatous case was treated with penicillin, 25,000 units every two hours for ten days. A total of 3,000,000 units was given. No good results were obtained. Similar results have been reported by Faget and Pogge." [See this *Bulletin*, 1945, v. 42, 646.]

PANJA, G. **Use of Penicillin in Rat and Human Leprosy.** *Indian Med. Gaz.* 1946, Aug., v. 81, No. 8, 306–7.

The treatment was of no benefit.

TISSEUIL, J. L'acide ascorbique est inefficace en injections intradermiques des taches de lèpre tuberculoide. [**Ineffectiveness of Intradermal Ascorbic Acid in Tuberculoid Leprosy.**] *Bull. Soc. Path. Exot.* 1946, v. 39, Nos. 7/8, 258–9.

FIGUEREDO, N. & DESAI, S. D. **Treatment of Tuberculoid Leprosy with Methylene Blue and Glucose.** *Leprosy in India.* 1946, Apr., v. 18, No. 2, 51–2.

"(1) Fifty-seven Nt_1 and 106 Nt_2 cases were treated with methylene blue 1 per cent. solution, *p*H7 [10 cc. intravenously twice each week], with an equal quantity of glucose 50 per cent. solution.

"(2) 77·2 per cent. of Nt_1 and 82·6 per cent. of Nt_2 cases showed improvement.

"(3) The improvement was seen in most cases after treatment for four months.

"(4) No case became worse."

TISSEUIL, J. Inactivité de l'huile iodoformée a 10 0/0 et action curative de l'huile de chaulmoogra iodée par voie intradermique dans les taches de lèpre tuberculoide. [**Inactivity of " Iodoform Oil " and Therapeutic Action of Intradermal Iodized Chaulmoogra in Tuberculoid Leprosy.**] *Bull. Soc. Path. Exot.* 1946, v. 39, Nos. 7/8, 259–61.

HELMINTHIASIS.

EINHORN, N. H. & MILLER, J. F. **Intestinal Helminthiasis : Clinical Survey of Six Hundred and Eighteen Cases of Infection with Common Intestinal Helminths in Children.** *Amer. J. Trop. Med.* 1946, July, v. 26, No. 4, 497–515. [15 refs.]

The data on which this study is based have been published before in five separate papers [this *Bulletin*, 1945, v. 42, 578, 911, 912 & 914, and 1946, v. 43, 577]. There is thus much repetition which is excusable only on the grounds that in this paper these five worm infections are compared to one another in all their aspects.

During the three years, 1941–1943, 518 children infected with intestinal parasites were admitted to the paediatric wards of the Gorgas Hospital (Panama Canal Zone). For the purpose of this analysis, to this number were added 100 out-patients infected with *Enterobius vermicularis*. Of these 618 children, 457 were infected with one species of worm, and 161 with worms of two or more species. The parasite infections discovered in the 518 hospital patients were ascariasis (247), ankylostomiasis (175), trichuriasis (153), oxyuriasis (115), and strongyloidiasis (44).

Analysis according to race (white, negro or mestizo), socio-economic level, and location of dwellings, three factors intimately linked, showed that oxyuriasis had a pedilection for the white child, of higher economic status, living in sanitary government quarters (80·5 per cent. of infections were in white children), whereas with ascariasis, trichuriasis and ankylostomiasis the reverse was the case and only 5·6, 6·0 and 5·6 per cent. of infections respectively were in white children. Poly-parasitism was largely confined to the mestizo living in the rural districts or insanitary outskirts of towns.

Age incidence varied with the different worms. Few infections were noted in the first year of life. The peak years for ascariasis were 1 to 3, for oxyuriasis 2 to 4, and for ankylostomiasis 6 to 9, but trichuriasis was fairly evenly distributed over the first nine years. Boys predominated except in the case of oxyuriasis (50 per cent.) and strongyloidiasis (45·4 per cent.), but of the latter there were only 11 cases with this infection alone.

The characteristic clinical feature of the various infections can be explained by considering the point of attack of each parasite. *Enterobius* produces symptoms by wandering outside the anal canal and irritating the surrounding skin, *Strongyloides* and *Trichuris* by irritating and damaging the bowel mucosa (diarrhoea), *Ascaris* by robbing the host of nutritious food (malnutrition), and by the larvae and adults invading vital organs, and the hookworm by ingesting the host's blood (anaemia). In poly-parasitism the picture is not so clear, but tends to assume the form associated with the dominant infection. Convulsions were observed only in ascariasis and oxyuriasis, on 11 occasions in all.

The blood picture was not characteristic in any infections ; there was usually anaemia in ankylostomiasis, and sometimes in severe strongyloidiasis and trichuriasis. The total leucocyte count remained within the normal range, and eosinophilia over 4 per cent. was noted in only 69 children (11·2 per cent.).

Hexylresorcinol and tetrachlorethylene were the most generally useful drugs and were very effective in ascariasis and ankylostomiasis, respectively. The other infections presented greater difficulties, but gentian violet was sometimes successful in strongyloidiasis and oxyuriasis, whereas *Leche de higueron* [obtained from the latex of a species of *Ficus*] was disappointing in trichuriasis when given by mouth, but in heavy infections it was effective as an enema.

L. E. Napier.

ZERCHANINOV, L. K. & BULYCHEVA, N. A. [**Helminthic Fauna of the Workers of Coal Mines.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1946, v. 15, No. 1, 66–7. [In Russian.]

The authors record the results of a helminthological survey among Ural coal-miners, 313 of whom were examined in 1940–1941 both by faecal smears and by Fülleborn's method. Helminthic infections were found in 35·6 per cent. distributed as follows: *Trichuris trichiura* 2·4, *Ascaris lumbricoides* 5·6, *Enterobius vermicularis* 14·7, Taeniidae 10·8, *Hymenolepis nana* 1·8, *Diphyllobothrium latum* 1·8 (the last-named infection was introduced from outside). The present findings are compared with the results of previous surveys among Soviet miners, which are set out in tabular form. In the case of the Ural miners, a considerably higher proportion were found to be infected with the Taeniid tapeworms, owing to their habit of consuming raw meat.

C. A. Hoare.

PINTO, C. Sôbre um foco de esquistosomíase mansoni em culturas de agrião (*Nasturtium officinale*) na cidade de Santos. [**A Focus of Schistosomiasis mansoni in Watercress Gardens in Santos (Rio de Janeiro).**] *Rev. Brasileira Med.* Rio de Janeiro. 1945, Oct., v. 2, No. 10, 820–23, 3 figs. English summary.

In a marshy, uncultivated area, close to the fine modern hospital of Santa Casa de Misericórdia, there are gardens for growing watercress (*Nasturtium officinale*) which is sold to the public and consumed locally in the Saboó quarter of the town of Santos. Examination of 1,126 persons, chiefly school-children, living there showed that 105 (9·3 per cent.) were passing ova of *S. mansoni*. The watercress was grown in shallow trenches into which was directed the faeces of the inhabitants, or the faeces were collected into a sunken receptacle which was then emptied into the trenches. Numbers of snails present were identified as *Australorbis glabratus*. Though 400 of these were dissected no evolutionary form of the schistosome could be detected; nevertheless, it is believed that it is through them that those who plant, gather or eat the watercress become infested.

H. Harold Scott.

PINTO, C. & DE ALMEIDA, A. F. Epidemiologia da esquistosomíase mansoni no Brasil. [**Epidemiology of *S. mansoni* in Brazil.**] *Rev. Brasileira Med.* Rio de Janeiro. 1945, Nov., v. 2, No. 11, 912–18, 2 graphs. [12 refs.] English summary.

Among the many persons whose occupations render them liable to infestation by *S. mansoni*—washerwomen, children playing in streams, operators engaged in bridge-building, railway constructors, topographers, engineers, fishermen, etc.—the authors mention those who work with the *guaxima* (*Eurema lobata*), a tree some 10 feet high, common in hot and moist climates. Workers with it stand for hours in water breaking it down to fibres; children as well as adults are occupied in this way. Another source of infection is the cultivation of

watercress. [On this one of the authors (C. Pinto) has written another paper, see above.] The intermediate hosts are *Australorbis olivaceus*, and *A. glabratus*. Examination of these snails in polluted canals of various municipalities of Minas Geraes revealed a high percentage with forked cercariae. Of more than 4,000 examined in Itambacurí, 45·5 per cent. were positive ; in one collection of 720 there were 584 infected (81 per cent.). *H. Harold Scott.*

JONES, Myrna F. & BRADY, F. J. **The Removal of the Cercariae of *Schistosoma mansoni* from Water by Filtration through Diatomaceous Silica in a Small Model Filter.** *Pub. Health Rep.* Wash. 1946, Oct. 25, v. 61, No. 43, 1538–43, 1 pl.

" Tests were made to determine the efficiency of a small model diatomaceous silica filter in the removal of the cercariae of *Schistosoma mansoni* from raw water. Cercariae added to the precoating solution were found to be present in the water passing the filter for as long as 12 minutes after the beginning of recirculation even though the filtered water appeared to be visibly free from turbidity within 1 minute after the beginning of recirculation.

" When the cercariae were added to the influent water after the diatomaceous silica had been deposited on the diaphragm, none was recovered in the effluent in any of nine experiments in spite of the use of three grades of diatomaceous silica, the use of low and high pressures, and the use of slow and rapid filtration rates."

COWPER, S. G. **Some Notes on the Maintenance and Breeding of Schistosome Vectors in Great Britain, with special reference to *Planorbis guadaloupensis* Sowerby.** *Ann. Trop. Med. & Parasit.* 1946, July, v. 40, No. 2, 163–70, 4 figs.

Dr. Cowper begins his paper by pointing out that any extensive programme of chemotherapeutic research on schistosomiasis, outside the endemic areas, involves the establishment of a vigorous stock of one or more species of the molluscan vectors. In addition, although not mentioned by the author, such strains are necessary for the study of conditions or substances likely to prove lethal to the snails or the cercariae escaping from previously infected specimens.

The reviewer has often been struck by the paucity of existing knowledge concerning even the most important molluscan vectors of disease, as compared with that concerning most arthropod vectors. Thus, *Fasciola hepatica* infection in sheep and cattle is common in Britain, and must cost this country, at a moderate estimate, not less than half a million pounds a year. Nevertheless, the literature concerning the vector, *Limnaea truncatula*, can only be described as meagre. Under these circumstances Dr. Cowper's notes on the technique of maintaining and breeding *Bulinus truncatus*, *Planorbis boissyi* and *Planorbis guadaloupensis*, together with his account of the bionomics of the last species, should prove of considerable value to workers in veterinary as well as in medical helminthology. *R. M. Gordon.*

CRAM, Eloise B. & FILES, Virginia S. **Laboratory Studies on the Snail Host of *Schistosoma mansoni*.** *Amer. J. Trop. Med.* 1946, Sept., v. 26, No. 5, 715–20.

" Nine additional species and subspecies of native American planorbids have been exposed to infection with *Schistosoma mansoni*, with negative results; additional attempts have been made to infect certain species which had been tested earlier.

" Additional laboratory studies have been conducted with a species of *Tropicorbis* which has proved susceptible to infection. To date, 9 specimens

have been infected ; all of these snails came, or were progeny of snails which came, from a lake on the campus of Louisiana State University at Baton Rouge, Louisiana. Subsequent to exposure of 22 wild adult specimens and of 77 laboratory-reared juveniles, 2 and 7 snails, respectively, or 9 per cent., shed cercariae of *S. mansoni*. On the other hand, there are described unsuccessful attempts to infect tropicorbids which, however, appear to be different species and which were collected from two different sites."

KIESER, J. A. Rooiwater (Bilharziasis). Beskrywing van 'n Geval met Dubbele Besmetting. [**Double Bilharzia Infection.**] *South African Med. J.* 1946, Oct. 26, v. 20, No. 20, 627–8, 1 fig. [Summary in English by the author.]

"1. A case of dual infection with *S. haematobium* and *S. mansoni* of the bladder and the rectum is described. The infection was contracted near Pretoria.

"2. The case history is not typical, and the probable cause of the symptoms was only revealed by an examination of the urine.

"3. All symptoms disappeared after a course of Fouadin injections, and the patient's weight increased considerably.

"4. The case was kept under observation for a year and showed no signs of recurrence."

BOECHAT, W. M. Apendicite esquistosomótica. [**Schistosoma Appendicitis.**] *Brasil-Medico.* 1946, Aug. 17, 24 & 31, v. 60, Nos. 33, 34 & 35, 277–80, 3 figs. [14 refs.] English summary.

The author recommends that in all cases of appendicitis, the stools should be examined for *S. mansoni*, *E. histolytica*, *Trichuris*, *Enterobius* and *Balantidium*.

Where these parasites are found, treatment directed to their elimination should be complementary to appendicectomy ; and where possible the diagnosis should be confirmed by histo-pathological examination of the appendix.

In support of these recommendations, the author presents clinical details of a patient in whose appendix *S. mansoni* was found. The histo-pathological changes are illustrated by three photographs. *H. J. O'D. Burke-Gaffney.*

HERNÁNDEZ MORALES, F., SUÁREZ, R. M., PRATT, Caroline K. & OLIVER GONZÁLEZ, J. **Treatment of Schistosomiasis Mansoni with Antimony Lithium Thiomalate (Anthiomaline).** *Puerto Rico J. Pub. Health & Trop. Med.* 1946, June, v. 21, No. 4, 336–43, 3 charts. [Spanish version 344–9.]

The authors set out to discover whether Anthiomaline (Merck) would produce a higher proportion of cures of *S. mansoni* infections than Fouadin and tartar emetic.

They treated 40 patients suffering from intestinal bilharziasis caused by *S. mansoni* with Anthiomaline, either in daily doses or every other day.

Anthiomaline is the antimony salt of lithium thiomalate, and the preparation used was made up in 3 cc. ampoules, containing 10 mgm. of trivalent antimony per cc. The drug was given intramuscularly in 3 cc. doses.

Sixteen patients were kept under observation in hospital, and twenty-four were treated in the out-patient clinic. Full records were kept, and the egg-content of the faeces was estimated by a technique devised by one of the authors, which adopts some of the features of the Stoll technique for hookworm ova. The technique, which involved counting the ova in the sediment of a strained suspension of faeces in water, is described in full.

Results of Anthiomaline Treatment of Patients infected with Schistosoma mansoni.

Number of Patients receiving Drug	Place of Treatment		Administration of Drug		Number of Patients in which Drug was Discontinued because of Toxic Reactions	Toxic Reactions	Amount Administered	Number of Days necessary for Disappearance of Ova, after Treatment was Commenced
	O.P.D.	Hosp.	Daily	Every other Day				
7		×	×		4	High fever in 1 Some fever in 2 Albuminuria in 2	24–45 cc.	10–33
9		×		×	4	Fever in 5 Congestion of conjunctival vessels in 3 Mild muscular and joint pains in all	20–48 cc.	10–11
24	×			×	4	General weakness in 1 Dizziness, headache, epigastric pain, and precordial discomfort in 1 Pronounced joint pains in 1 Bradycardia of 46 beats per minute in 1	12–45 cc.	Not determined

All but one of the 16 hospital patients were males between 14 and 28 years. Daily doses of Anthiomaline were given to 7 of them, and in 9 patients it was administered every other day. After preliminary trials with 2 cc., the initial dose was standardized at 3 cc.

In the case of the group of 9 patients (treated on alternate days) no serious toxic reactions were observed. The reactions seen were slight pyrexia (5); some conjunctival congestion (3); mild muscular and joint pains (all).

Only 3 of the 7 patients receiving the drug daily were able to tolerate the total dose of 45 cc. The toxic reactions noted were fever between 100°–103°F. (3), and slight albuminuria (2), after 24 to 36 cc.

The 24 out-patients also received 3 cc. every other day. Four patients were unable to complete the course: owing to general weakness (1); dizziness, headache, epigastric pain and praecordial discomfort (1); pronounced joint pains (1); and bradycardia (1) after 28, 12, 24 and 36 cc. respectively.

A progressive eosinophilia (53 per cent. in two cases) was noted during treatment.

The results are summarized in the table above.

The author concludes that Anthiomaline, in 3 cc. doses intramuscularly every other day, is markedly parasitotropic against *S. mansoni*, and rarely produces toxic reactions of a serious nature. *H. J. O'D. Burke-Gaffney.*

HALAWANI, A. & ABDALLAH, A. **Intensive Treatment of Schistosomiasis with Repodral. A Preliminary Report on Fifteen Cases.** *J. Roy. Egyptian Med. Ass.* 1946, Mar. & Apr., v. 29, Nos. 3/4, 101–21.

A number of intensive methods for shortening the course of treatment of schistosomiasis with antimony have been devised, and these include the use of different preparations, increasing the size or frequency of the dose, or altering the route of administration.

The authors quote MILLS [this *Bulletin*, 1946, v. 43, 346] who gave Stibophen (B. W. & Co.) [=Fouadin, Bayer] or Anthiomaline (M. & B.) for six days during two successive weeks; and ALVES and BLAIR [this *Bulletin*, 1946, v. 43, 344] who used sodium antimonyl tartrate three times daily in intravenous injections at three-hourly intervals on each of two successive days. These workers considered that slow and steady injection was of fundamental importance; there was a striking absence of the more troublesome effects of intravenous injections of antimony, but occasionally moderate reactions were encountered.

The present authors have employed Repodral (Winthrop, U.S.A.) in the intensive treatment of schistosomiasis. This preparation is stated to be identical with Fouadin and to contain "13·5 per cent. of antimony, hence 1 cc. of the 6·3 per cent. solution represents 8·5 mgm. of trivalent antimony."

The authors found by experiment that the total dose required for intensive treatment was about 0·5 cc. per kgm. of body weight. They gave it in 6 injections of 5 cc. each at three-hourly intervals three times daily on two successive days, thus administering a total dose for an adult weighing 60 kgm. of 255 mgm., as compared with 264 mgm., which is the amount "present in 12 grains of sodium antimonyl tartrate."

This treatment was given to 15 selected adult males suffering from *S. haematobium* infections. Liver and kidney function tests, and electrocardiograph investigations were made before treatment began. The urine was examined daily for a month and all laboratory examinations were repeated two weeks after treatment, since it was found that sometimes living ova disappeared after eleven days.

Cure was obtained in 11 (73·5 per cent.) of cases. Alves and Blair obtained 100 per cent. cure by means of their intensive method. The present authors

consider nevertheless that Repodral is less toxic than tartar emetic, and fear that, with the prevalence of bilharzial cirrhosis and nutritional deficiencies in Egypt, the average Egyptian patient might not tolerate intensive treatment with the latter drug.

The four cases which were not cured improved considerably.

Toxic symptoms were not severe, and in no case did reactions cause the treatment to be abandoned. No deleterious effect on previously normal livers or kidneys, nor on the pulse rate and blood pressure, were observed.

The results of treatment are summarized in a table, and detailed case-histories of all 15 patients are given. *H. J. O'D. Burke-Gaffney.*

HAMMOUDA, M. **Intensive Treatment of Bilharzia with Repodral and the Care of the Heart.** *J. Roy. Egyptian Med. Ass.* 1946, Mar. & Apr., v. 29, Nos. 3/4, 122–7, 2 figs.

The author studied the hearts of those patients treated with Repodral by HALAWANI [above].

The drug was first given to dogs in conditions identical with those employed in the case of human patients. E.C.G. readings were taken and repeated after each day's treatment. Changes were slight and transient, both during rest and after severe muscular exercise.

In the case of human patients, treatment was only begun when the patient, who was kept in bed, showed normal liver and kidney function and a haemoglobin percentage of over 60. E.C.G. readings were taken during rest and after standard exercise. Treatment was commenced and, after the two days' course of Repodral, the patient was brought by ambulance for the E.C.G. readings which were again taken during rest and after exercise. He was not allowed to walk until the E.C.G. reading became normal, which usually took 4 or 5 days.

The results appeared to be very satisfactory when these precautions were taken. Two tables illustrate typical E.C.G. readings in dogs and men. The author tried Repodral treatment controlled by E.C.G. readings, on two schoolboys, aged 12 and 15 years, who were suffering from haematuria, with schistosome ova in the urine. The results were satisfactory, the urine becoming free from living ova on the 12th day. "They both supported the treatment very well without nausea and vomiting." *H. J. O'D. Burke-Gaffney.*

CAWSTON, F. G. **The Control of Schistosomiasis with due consideration of the Destruction of Larvae.** *Acta Med. Scandinavica.* 1946, Nov. 9, v. 126, Nos. 2/3, 237–40, 1 fig.

DICKMANN, G. H. Cisticercosis de la fosa craneana posterior (4 casos). [**Cysticercosis of the Posterior Cranial Fossa.**] *Prensa Méd. Argentina.* 1946, Aug. 9, v. 33, No. 32, 1628–38, 6 figs. [28 refs.]

Human cysticercosis is much rarer in the Argentine than in some parts of America, Chile and Mexico for example. The author has been able to find only 11 cases recorded of extraneural localization and 10 of invasion of the central nervous system. Of the latter, 6 were discovered at autopsy, 2 by lumbar puncture and 2 at operation. Of course, if they are cretified X-rays would demonstrate them.

He now puts on record four cases under his own observation, none diagnosed before operation; three showed free vesicles in the cisterna magna and the other in the fourth ventricle. There are no distinctive clinical signs; epileptic and apoplectic fits, psychic disturbances and meningeal symptoms are not peculiar to cysticercosis. The colloidal benzoin reaction is positive in this but

also in cases of cerebral tumour, in disseminated sclerosis, encephalitis, etc. Eosinophilia of the cerebrospinal fluid, with hypo-albuminosis, increase of leucocytes and negative Wassermann reaction are suggestive.

Of the four cases detailed, one was in a student of 18 years and his condition was cured by operation ; others were a man of 33, who died some 7 weeks after operation ; a man of 38, who became practically normal after the operation, the only residual signs being occasional vomiting and headache ; the fourth was a cattle-dealer, 26 years of age, who also made a good ultimate recovery. He had exhibited Burns's symptom of headache, nausea and vomiting on standing, partially or completely relieved on lying down. *H. Harold Scott.*

WATSON, J. M. **Helminths Infective to Man in the Syrian Hamster.** [Memoranda.] *Brit. Med. J.* 1946, Oct. 19, 578. [10 refs.]

STUNKARD (*J. Parasitology*, 1945, v. 31, 151), recently reported the presence of *Hymenolepis nana* eggs in the faeces of a batch of Syrian hamsters (*Cricetus auratus*) obtained for experimental purposes. This parasite occurs commonly in rats and mice, and ova from this source have been used successfully to infect man. A human infection may reach serious proportions because of internal auto-infection, since *H. nana* is directly infective to man and does not require an intermediate host.

Stunkard therefore stressed the risk of infection in laboratory workers engaged in handling Syrian hamsters, which are increasingly used experimentally in the study of a number of infective diseases.

In view of these findings, the present author examined *post mortem* a number of hamsters used for experimental infection of kala azar in the Wellcome Laboratories of Tropical Medicine in London.

From 160 animals, *H. nana* was found in 19 (11·9 per cent.). Some of them were fairly heavily infected (in one case, 22 adult worms were found). Also, 83 animals (51·9 per cent.) were infected with the oxyurid nematode, *Syphacia obvelata*, which has also been reported to be infective to man, though this type of infection is less certain than that with *H. nana*.

Because of possible human infection by faecal contamination from these hamsters, all four persons concerned in handling them were examined.

Two stool samples and seven " cellophane " swabs, as described by HALL [this *Bulletin*, 1937, v. 34, 878], were taken from each person and examined respectively for ova of *H. nana* and *S. obvelata*.

All the specimens were negative : and since no special precautions had been taken in handling the hamsters, it would seem that the risk of infection to laboratory workers and to animal-house staff is not great.

H. J. O'D. Burke-Gaffney.

LARSH, J. E., Jr. **A Comparative Study of *Hymenolepis* in White Mice and Golden Hamsters.** *J. Parasitology.* 1946, Oct., v. 32, No. 5, 477–9.

" The host relationships of *H. nana* var. *fraterna* were compared in white mice and golden hamsters. The hamsters showed a greater percentage development of adult worms, and their length at eleven days was much greater than those in mice. As was expected from this rate of growth, the prepatent period of the worms was shorter in hamsters. The patent period, likewise, was much shorter in hamsters."

BRISOU, J. Diagnostic du kyste hydatique par extrait de ténia. [**Diagnosis of Hydatid Cyst with *Taenia* Extract.**] *Bull. Soc. Path. Exot.* 1946, v. 39, Nos. 5/6, 193–6.

The author records the results of his use of extracts of tapeworm material for skin tests for the presence of hydatid cysts. He points out that recent work,

most of which has been abstracted in this *Bulletin*, indicates that extracts of many different species of tapeworm may be used, because group reactions occur. The author washed the cestode in running water, rinsed it in sterile water, dried it at 37°C. for 24 to 48 hours and titrated the dried material, making a 1 per cent. suspension of the powder thus obtained in normal saline phenolized to 0·5 per cent. This suspension was kept at 37°C. for 2 hours and then centrifuged, the supernatant fluid being used as the antigen, of which 0·1 cc. was injected under the skin, controls being done with normal saline phenolized to 0·5 per cent.

Reactions were sometimes immediately positive and were always more intense than those obtained with hydatid fluid ; they also persisted longer and were often pruriginous. Some positive reactions were obtained in subjects from whom the " Taenia " had been removed more than six months previously.

The author analysed the antigen chemically and found in it :—

1. A protein fraction precipitated by trichloracetic acid ;
2. A polysaccharide fraction, which is the most important element in the antigen. This gives a strongly positive Molisch reaction, is insensitive to acid hydrolysis, but is easily decomposed by emulsion.

" This fraction contains, after hydrolysis, 40 per cent. of reducing sugar expressed as glucose." The author quotes work which records the isolation of polysaccharide substances from *Ascaris lumbricoides*, *Necator americanus*, *Trichinella spiralis*, *Schistosoma mansoni*, *Cysticercus cellulosae*, the larval stages of *Taenia solium* and other species [*cf.* OLIVER-GONZÁLEZ and TORREGROSA, this *Bulletin*, 1945, v. 42, 45 : CULBERTSON and ROSE, *ibid.* 1942, v. 39, 95, and other papers abstracted in this *Bulletin*.]

The author then very briefly discusses the relationships between antigens derived from helminths and the blood-group iso-agglutinins [*cf.* the more detailed discussion of this subject by OLIVER-GONZÁLEZ, below, p. 226].

The author's general conclusions are that it is possible to obtain from any species of cestode an antigen of known strength which can be used for skin tests. Its specificity is of the same order as that of antigen obtained from hydatid fluid, but it is stable and produces positive reactions which are usually strong and easy to read ; but it is necessary to know whether the subject had suffered previously or not from " taeniasis ". The essential part of this antigen is the polysaccharide fraction joined to a distinct protein fraction, so that it has a composition similar to that of various other helminth antigens and to that of erythrocytes and even of certain bacilli (*e.g.* the Shiga bacillus) or of blood parasites. *G. Lapage.*

SHAW, H. M. **A Case of Hydatid Disease of the Thyreoid Gland.** *Med. J. Australia.* 1946, Sept. 21, v. 2, No. 12, 413–14, 1 fig.

BADO, J. L. Apuntes sobre equinococosis osea. [**Echinococcal Cysts of Bone.**] *Día Médico.* 1946, June 24, v. 18, No. 25, 762–4, 766.

Fortunately, localization of *Echinococcus* in bony structures is rare, for treatment is difficult and often unsatisfactory. It used to be said that if bone was affected other structures and organs escaped, but this is not true. When bones are invaded the commonest sites are the upper ends of the femur, tibia or humerus, the vertebrae and the ribs. The primary site may, however, be diaphysis or epiphysis, whence growth, slow and insidious, progresses. In the former case, in its growth it causes destruction of the trabeculae, molecular necrosis, thinning of the bone and finally spontaneous fracture. If the epiphysis is invaded, the interarticular cartilages usually escape and the tumour is hour-glass-shaped, passing over to invade the epiphysis of the contiguous bone.

Growth is very slow. Biological tests are not very reliable and the best diagnostic means is X-rays and as a last resource puncture [but there is a grave risk of tearing up the wall and dispersion of the scolices]. The only treatment is surgical, and for successful results that must be undertaken as early as possible.

H. Harold Scott.

PETERSON, J., ARBONA, G. & ACOSTA, Josefina. **Hookworm Infestation in a Small Town of Puerto Rico.** *Puerto Rico J. Pub. Health & Trop. Med.* 1946, Sept., v. 22, No. 1, 48–57, 2 charts. [Spanish version 58–65.]

KAMALOV, N. G., GORDADZE, G. N., TSUTSUNAVA, T. N., KHIZANISHVILI, A. O., KAMALOVA, A. G. & BUGUIANISHVILI, S. M. [**Sanitary Measures in a Focus of Ankylostomiasis.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1946, v. 15, No. 1, 55–65, 5 figs. [In Russian.]

The authors have undertaken an anti-helminthic campaign in a selected village of Georgia, representing an endemic focus of ankylostomiasis. The total incidence of helminthic infection among the 771 inhabitants of this village was 97·3 per cent., of whom 64·9 harboured ancylostomids, 82·8 ascarids and 89·5 *Trichuris*. The mean density of invasion with hookworms was 548 eggs per 1 gm. of faeces. The main epidemiological factor in the village was the constant contamination of the soil, due to almost complete absence of proper latrines, to dissemination of hookworm eggs and larvae by domestic animals, and by abundant and frequent rains, as well as to fertilization of kitchen gardens and orchards with fresh faeces. The campaign against hookworm disease consisted, on the one hand, of improvements in sanitation, chiefly by provision of well-planned latrines, and, on the other hand, of drug-treatment. The latter was carried out exclusively with carbon tetrachloride, which had a good therapeutic effect. As a result of these measures there was a sharp drop in the incidence of hookworm infection: from 64·9 per cent. in December 1937 to 23·1 in May 1938; to 10·1 in December 1938; to 3·1 in December 1939; and finally to 6·5 in December 1940; while the mean number of ova per gramme of faeces for the same periods was 548, 102, 48, 49 and 62. *C. A. Hoare.*

WRIGHT, D. O. & GOLD, E. M. **Löffler's Syndrome associated with Creeping Eruption (Cutaneous Helminthiasis). Report of Twenty-Six Cases.** *Arch. Intern. Med.* 1946, Sept., v. 78, No. 3, 303–12, 3 figs. [Refs. in footnotes.]

In August 1945 the authors published an account of nine cases of Löffler's syndrome associated with creeping eruption, thought to be due to larvae of *A. braziliense* of which the natural hosts are the dog and the cat [see this *Bulletin*, 1945, v. 42, 1041]. They now put on record 17 more, making 26 instances in which the Löffler syndrome has been found by them among a total of 76 cases of creeping eruption.

Blood smears examined every third day showed an eosinophil range up to 51 per cent., and in the sputum up to 90 per cent.; in each the degree ran fairly parallel with the pulmonary consolidation, but persisted after the lung signs subsided. The pulmonary infiltrations were patchy and also migratory. In no case were helminthic ova present in the faeces (one had *Necator americanus* ova, but the pulmonary signs did not develop in this man) nor in the sputum in the course of 381 examinations.

Three possibilities are suggested in explanation of the association:—

1. That the pulmonary infiltrations result from larval migration in the lungs.
2. That the larvae reach the lungs and die there, and hence do not reach the bowel and are not found in the faeces.

3. That, since the intradermal reaction to *A. lumbricoides* and *Trichinella spiralis* are positive, the lung infiltrations are due to allergy to blood-borne antigens from the larvae in the skin.

The absence of larvae from stools and sputum lend support to the third view.

H. Harold Scott.

PIERAERTS, G. Étude sur le syndrome dépigmentation-oedème au Kasai. [**A Syndrome of Pigmentation and Oedema in Kasai.**] *Bull. Soc. Path. Exot.* 1946, v. 39, Nos. 5/6, 226–35. [48 refs.]

This is in the main a recapitulation of the views expressed by the author in 1942 [see this *Bulletin*, 1942, v. 39, 99, and 1943, v. 40, 406]. That paper was outstanding for its observations on the distribution of the disease "*diboba*", and on the relation between incidence and food supply. The disease is found in the Belgian Congo and is characterized by anaemia, oedema and depigmentation of the skin and hair. It is considered to be identical with the condition described in East Africa by GILLAN [see this *Bulletin*, 1935, v. 32, 71], TROWELL (1937) and others, but to be slightly different from kwashiorkor in West Africa, for references to which see GELFAND, below, p. 232. [The basis for this distinction is not clear, since in both the West and East African diseases there is anaemia, oedema and depigmentation. Dermatosis is a prominent part of both syndromes, whereas in "diboba" skin lesions are usually absent, or if present are considered to be secondary and non-specific.]

In discussing the aetiology of "diboba", the author states that iron, or an iron-copper complex, acts as a coenzyme for the production of melanin by dopa-oxidase. In this way depigmentation is related to anaemia, and both to iron deficiency. The latter is the combined result of defective intake and ankylostomiasis. It is recognized, however, that it is not only iron which is lacking; the absence of protein from the diet is the "generic characteristic", as the author puts it, of this and allied deficiency states.

[No references are given to support the statement that iron plays a part in melanogenesis. The theory that the syndrome is caused by iron deficiency was suggested by the empirical finding, reported in the author's earlier paper, of the return of normal pigmentation, as well as improvement in anaemia and oedema, as a result of treatment with iron and anthelminthics.]

J. C. Waterlow.

SWARTZWELDER, J. C. **Clinical Ascariasis. An Analysis of Two Hundred and Two Cases.** *Amer. J. Dis. Children.* 1946, Aug., v. 72, No. 2, 172–80.

Ascariasis is relatively common in New Orleans: of 11,000 stools examined by the author and his colleagues, 426 contained the ova of *Ascaris lumbricoides*. An analysis is made of the data from 202 Charity Hospital patients in whom *Ascaris* was the only parasitic infection (a few with light *Trichuris trichiura* infections were not excluded) and in whom all the symptoms could be attributed to this infection.

Of the 202 patients, 170 were under 16 years of age and 76 were under 6; the age group showing the maximum was that between 2 and 3 years, in which there were 33 patients. Fifteen patients were over 30 years of age.

Thirty per cent. were Negroes, whereas about half the patients in the Charity Hospital are Negroes. There is thus an actual predominance of white patients; this observation surprised the author, but is in keeping with his experience with clinical trichuriasis in this area [see SWARTZWELDER, this *Bulletin*, 1940, v. 37, 660]. There was no significant sex or seasonal distribution.

The chief complaints for which the patients were admitted to hospital were: abdominal pain or discomfort (112); passage of worms (35); fever (34); vomiting (32); convulsions (19); cough or cold (16); diarrhoea (11); and constipation (9). Fifteen other complaints are listed; these include jaundice and haemoptysis (once each).

The predominant physical signs observed in hospital were: rise of temperature (98); abdominal pain (71); abdominal distension (50); abnormal pulmonary conditions (23); abdominal rigidity (9); and palpable mass in abdomen (9).

The abdominal pain usually appeared suddenly and was most frequently in the epigastrium or the region of the umbilicus, but in 17 cases it was in the right lower quadrant.

The fever was above 101°F. in 33 cases; respiratory signs were absent in most of these. The temperature was between 99·1 and 101°F. in 65 cases.

Intestinal obstruction occurred in 18 cases, in 16 of these prior to treatment. Six of these patients died, two following treatment (santonin and carbon tetrachloride).

Tentative diagnoses included: intestinal parasites (117); *Ascaris* infection (42); chronic recurrent appendicitis (35); infection of upper respiratory tract (18); gastro-enteritis (16); intestinal obstruction (14); and tuberculosis (10). Twenty-nine other diagnoses were made, but none more than 7 times: these included epilepsy (7), typhoid (2), malaria (2), and neuro-circulatory asthenia (1).

The red cell counts and haemoglobin estimations were done only in 30 and 22 cases respectively, but the patients were not representative of the group. Anaemia was not a striking feature.

In 64 white blood cell counts, the total count exceeded 10,000 per cmm. in 14; in 12 the eosinophil percentage exceeded 6, and in 36 cases it was less than 3 per cent. The maximum eosinophil count was 28 per cent.

L. E. Napier.

OLIVER-GONZÁLEZ, J. **Functional Antigens in Helminths.** *J. Infect. Dis.* 1946, May–June, v. 78, No. 3, 232–7, 1 fig. [10 refs.]

Earlier work quoted by the author has shown that the antigens which produce immunity against nematode infestations are only a few of those which are present in the nematodes and that these other antigens play no part in the production of the immunity. In this paper the author describes his investigation of the functions of the non-immunizing antigens present in *Ascaris lumbricoides*. He has shown [this *Bulletin*, 1944, v. 41, 223], by means of the precipitates formed around larvae of *A. lumbricoides* placed in immune sera, that the antigens which provoke anti-parasitic factors against *A. lumbricoides* are apparently present only in the egg-tissue of this species and not in the material obtained from its cuticle, sperm, muscle, intestine and coelomic fluid.

For the present work male rabbits only were used, weighing 3,000 to 4,000 gm. and also male and female guineapigs weighing 300 to 400 gm. The agglutination tests were done by mixing "0·1 ml. of undiluted serum and of serum, diluted 1 : 2, 1 : 4, 1 : 8 etc." with equal volumes of 2 per cent. suspension of washed erythrocytes freshly obtained and washed three times in normal saline. The mixtures were put in the water-bath at 37°C. for 30 minutes and then overnight in the ice box at 6°C. The agglutination titres were then ascertained by microscopic examination of the mixtures after exposure at temperatures of 37° and 6°C. respectively.

Precipitin titrations were carried out by the disk technique, using undiluted sera overlaid with dilutions of 1 : 100, 1 : 200, 1 : 400, 1 : 800, etc. of the adult

Ascaris antigen. The dried tissues and infective eggs were obtained by the technique described by González (*loc. cit.* above).

Experiment 1 was designed to elucidate the effect of infestation with *A. lumbricoides* on rabbit blood agglutinins. The rabbits used lacked Group A substance in their erythrocytes. Four rabbits were given 20,000 infective eggs of *A. lumbricoides* by stomach tube and 35 days later were re-infested with another dose of 20,000 or more eggs. They were bled 7 days before the first dose of eggs and every 7th day throughout the experiment. The sera obtained were tested for α1, α2, β and anti-O iso-agglutinins and for cold agglutinins. Precipitin titres of the sera were also determined with extract of whole *A. lumbricoides*. During the 35 days after the first dose of eggs there were no significant changes in the titres of the α1 and α2 agglutinins, but these were markedly increased after the second dose of egg *e.g.*: the α1 titre rose from 1 : 64 to 1 : 65,536 on the 7th day after re-infection with the second dose of eggs and the α2 titre rose from 1 : 16 to 1 : 2,048. Precipitin reactions to extract of whole *Ascaris* rose from the 7th day after the first dose of eggs and remained high. The titres of the β and anti-O agglutinins were not significantly altered throughout. The titres of the agglutinins of the normal rabbit sera used were low.

Before the cold agglutinins could be studied the α1, and α2, β and anti-O agglutinins which act at 37°C. had to be absorbed from the sera. This was done by treating the sera with fresh erythrocytes of the homologous groups; but no significant increase of the cold agglutinins could be detected after the two doses of *Ascaris* eggs and there was no significant variation of the titres of the cold agglutinins for the various blood groups.

For tests of the absorption of iso-agglutinins and cold agglutinins with isolated tissues of *A. lumbricoides* enough dried and powdered material from the various tissues of *Ascaris* (cuticle, sperm, muscle, intestine and coelomic fluid) was added to small portions of rabbit sera to make 4 per cent. suspensions. These mixtures were incubated at 37°C. for 1 hour, shaken often and left in the ice box overnight. It was found that treatment of the sera with cuticle material reduced the titres of the α1, α2 and β agglutinins, but the material from the other tissues had no effect. But each tissue reduced to the same extent the titres of the cold agglutinins for A, B and O cells.

For the detection of anaphylactogen in ascarid tissues 12 guineapigs divided into 6 lots were fed by stomach tube with 5,000 infective eggs of *A. lumbricoides*. On the 8th day after feeding these an intravenous injection of an extract of one of the *Ascaris* tissues mentioned above was given to each of the guineapigs. Intraperitoneal injections of 5 ml. of serum from rabbits artificially immunized with whole adult *Ascaris* material (passive sensitization) were given to 12 other guineapigs and 48 hours after the injection of this anti-ascarid serum the guineapigs were given intravenous injections of extracts of the various *Ascaris* tissues, just as the other 12 were. When coelomic fluid or extract of intestine material was injected, anaphylactic reactions (restlessness, sneezing, roughing of the fur, discharge of urine and faeces) were observed in all the guineapigs sensitized to *Ascaris* either by injection or by passive sensitization, the reactions produced by the coelomic fluid being the more severe (one guineapig died from shock); but no anaphylactic reactions were observed when extracts of the other tissues (cuticle, muscle, sperm and egg) were injected.

Discussing his results the author points out that Campbell (*J. Infect. Dis.*, 1939, v. 65, 12) isolated a polysaccharide substance from *A. lumbricoides* which acts as a complete antigen, and that González (*J. Infect. Dis.*, 1944, v. 74, 81) isolated a polysaccharide substance immunologically similar to the substance which determines the blood groups of man from *A. lumbricoides*, *Trichinella spiralis*, *Schistosoma mansoni* and *Necator americanus*, which, when it is added to human sera, inhibits the α and β agglutinins.

González claims that the experiments described above indicate that rabbits infested with *Ascaris* are not immunized against this substance after a first infestation, but are immunized against it after a second infestation. The β and anti-O agglutinins were, however, not altered. Although the α2 agglutinins of man are not specific for A2 cells but also react with all Group O erythrocytes, no reaction was noted between the agglutinins in rabbit serum and the Group O cells. The reaction of the α2 agglutinins is, however, more intense with A2 than with O cells, so that it is possible that repeated reinfestation would have revealed a reaction with the O cells.

Although the polysaccharide isolated from *Ascaris* inhibits β agglutinins as well as α1 and α2 agglutinins in human sera, it had no effect on the titre of rabbit β agglutinins. The reason for this may be that the polysaccharide is common to both A and B agglutinogens, but that infestation produces agglutinins against A substance only. This was suggested by the author (OLIVER-GONZÁLEZ, *J. Infect. Dis.*, 1944, v. 74, 81), who surmised (*Proc. Soc. Exper. Biol. & Med.*, 1944, v. 57, 25) that an iso-agglutinogen-like substance may be present in the malarial parasite. Immunization of the host may then cause the development of auto-agglutinins for the host's erythrocytes, the agglutination of which may be followed by intravascular haemolysis "as observed in blackwater fever." The author discusses the interesting observations that the increase of the iso-agglutinin titre "during infection with animal parasites" seems to be limited to the α1, and α2 agglutinins, just as it is in rabbits infested with *Ascaris*, and the fact that blackwater fever occurs to a higher degree in certain families. He suggests that the occurrence of blackwater fever may be explained on a basis of blood groups. Because immunization of the host with the iso-agglutinogen-like substance may lead to the formation of homologous α1 and α2 agglutinins, auto-agglutination and haemolysis would occur in individuals with the blood agglutinogens A1, A2 and O. If the iso-agglutinins lead to pathological changes only among individuals of certain blood groups during infection of man with various organisms, the relationship between the genetic constitution and natural immunity may be better understood; and individuals with a genetic constitution for specific agglutinogens will be the most susceptible to the pathological changes associated with the infection.

The author's failure to obtain an increase of cold agglutinins during infection with *Ascaris* agrees with the findings of other workers. DAMMIN and WELLER [this *Bulletin*, 1945, v. 42, 941] found that the titre of cold agglutinins did not exceed 1 : 10 in 303 out of 312 (97 per cent.) of subjects with schistosomiasis, filariasis and malaria, and cold agglutinins have only been reported regularly in trypanosomiasis (see YORKE, *Ann. Trop. Med. & Parasit.*, 1911, v. 4, 509). Powerful cold agglutinins have, however, been reported without infection.

During the above experiments each of the tissues of *Ascaris* partially absorbed the cold agglutinins and it is possible that if more *Ascaris* substance had been added the cold agglutinins would have been completely absorbed.

The above results show that the coelomic fluid is the tissue which seems to be the most closely associated with anaphylaxis in the guineapig and it is important to find out whether the coelomic fluid is also associated with human hypersensitivity to *Ascaris*. *G. Lapage.*

HERNÁNDEZ MORALES, F. & GONZÁLEZ BARRIENTOS, G. **The Incidence of Filariasis at the Insular Penitentiary for Men.** *Puerto Rico J. Pub. Health & Trop. Med.* 1946, Sept., v. 22, No. 1, 99–101. [Spanish version 102–5.]

"In a filariasis survey, conducted at the Insular Penitentiary for Men, night blood was obtained from 1,256 inmates and subsequently examined. Microfilariae were found in 57, or 4·35 per cent., of them.

"Of the 57 positive cases, 40 were submitted to a physical examination in order to determine what evidences of filariasis there might be among them. Elephantiasis of the scrotum was observed in 1 and moderate thickening of the spermatic cord in another; whether or not this was of filarial origin is not conclusive. However, evidence of hydrocele was conspicuous in this group and in the 1,199 inmates negative for microfilariae. Only 9 histories of lymphangitis were obtained for the total group, however.

"If elephantiasis of the scrotum, thickening of the spermatic cord, recurrent attacks of lymphangitis, and hydrocele are considered evidence of filariasis, then the total incidence of the disease among the 1,256 prisoners examined was 13·6 per cent."

HERNÁNDEZ MORALES, F. & OLIVER GONZALEZ, J. **Filariasis in Puerto Rico. A Note on Family Incidence.** *Puerto Rico J. Pub. Health & Trop. Med.* 1946, Sept., v. 22, No. 1, 95–6. [Spanish version 97–8.]

NELSON, E. C., WEBB, J. E., BAYLISS, M. & STARKEY, G. S. **Studies of Filariasis. Development of** *Wuchereria bancrofti* **in** *Culex quinquefasciatus* **of Oahu.** *Amer. J. Trop. Med.* 1946, Sept., v. 26, No. 5, 707–13, 14 figs.

"Microfilariae of *Wuchereria bancrofti* from Okinawa develop readily into infective larvae in *Culex quinquefasciatus* of Oahu, Territory of Hawaii. Microfilariae of *Wuchereria malayi* from Koreans failed to develop in the same mosquito."

CULBERTSON, J. T. & PEARCE, Elizabeth. **Chemotherapy of Filariasis** (*Litomosoides carinii*) **in the Cotton Rat by the Administration of Stibanose (Solustibosan).** *J. Pharm. & Exper. Therap.* 1946, June, v. 87, No. 2, 181–4, 1 fig.

"The filaria (*Litomosoides carinii*) of the cotton rat can be eradicated from these animals by the repeated administration of the pentavalent antimony compound stibanose (or solustibosan). Because of the excellent tolerance man is known to have for this drug, its trial in the chemotherapy of human filariasis is strongly indicated."

DUBOIS, A. Prurigo et *Loa loa.* [**Prurigo and** *Loa loa.*] *Ann. Soc. Belge de Méd. Trop.* 1946, June 30, v. 26, No. 2, 109–10.

The occurrence of prurigo in two Europeans in the Belgian Congo was shown to be associated with *Loa loa* infestation. The first patient had been living, since 1932, in an area (Népoko) where *L. loa* is common. He had never had classical features of infection, nor was the parasite found, but in 1935 he had a huge swelling of the arm.

Since 1943, he suffered from nocturnal itching and fleeting urticarial eruptions. No *Onchocerca* was detected. Microfilariae of *Loa* were found in skin scarifications and in the blood. There was a 15 per cent. eosinophilia. Various forms of treatment produced little benefit.

The second patient lived in the same area. He had suffered from filarial oedema for 4 or 5 years, but had not had any for several years past. He once had a passing filarial infection in his eye. He had experienced pruritus since 1936. At the end of 1945, he showed a typical prurigo in the back and chest with considerable thickening of the skin. Examinations for *O. volvulus* were consistently negative. No parasites of any kind were found in a thick blood film.

In April 1946, thick films and centrifuged specimens of blood were still negative. There was a 21 per cent. eosinophilia. Treatment by various means was not satisfactory.

The author points out that whilst it is difficult to exclude all the possible causes of the skin conditions, it is noteworthy that they were " subsequent to the development of the worm and, in the second case, persisted after every other sign of infestation, except, perhaps, the eosinophilia."

H. J. O'D. Burke-Gaffney.

CABALLERO y C., E. Estudios helmintologicos de la region oncocercosa de Mexico y de la Republica de Guatemala. *Nematoda* 3a parte. *Filarioidea.* II. El genero, Onchocerca. [**Helminthological Studies in Mexico and Guatemala: Onchocerca.**] *An. Inst. Biol.* Mexico. 1945, v. 16, No. 2, 367–409, 1 text fig. & 39 figs. on 3 pls. [Bibliography.]

This includes details of *O. volvulus.*

VEGA, C. Anotaciones Bibliográficas acerca de la Oncocercosis en México y Guatemala 1917–1945. [**A Bibliography of Onchocerciasis in Mexico and Guatemala, 1917–1945.**] 20 pp. 1946. Mexico : Universidad Nacional Autonoma de Mexico.

A useful bibliography of some 150 references.

OELKERS, H. A. & ZESSLER, H. Pharmakologische Untersuchungen an Oxyuren. [**Pharmacological Studies on** *Enterobius.*] *Arch. f. Exper. Path. u. Pharm.* 1942/43, v. 200, 518–27. [12 refs.]

See this *Bulletin,* 1942, v. 29, 709.

LEHMENSICK, R. Ueber die Trichinose in der freien Wildbahn. (Weiterer Beitrag zur Epidemiologie der Trichinose). [**Trichiniasis in Non-domesticated Animals.**] *Zent. f. Bakt.* I. Abt. Orig. 1942, Dec. 8, v. 149, No. 6, 338–44, 1 fig.

It is well known that man becomes infested with Trichinella from eating trichinosed pig-meat, but the knotty question is: How does the pig become infective ? The author maintains that the infection is common among wild animals—foxes, badgers, wild boars—and that they transmit it to house rats and mice occasionally and these in turn may be devoured by the pig and through its flesh man becomes infested. He, therefore, arranged through the local huntsmen to have sent to him parts of any fox killed, these parts to include especially the diaphragm and the base of the tongue. These were then examined by the trichinoscope and if none was seen, rats were fed with the material. A month later, the rats were killed and examined for trichiniasis. Of 137 sent thus from the Rhineland three were microscopically positive and two others set up infection in rats, *i.e.* 3·4 per cent. were positive. Also, of 66 foxes sent in from other districts 10 were infested [the table states 11, but the addition is wrong] and of the other 56 " 2 or 3 more " were found infested. Another table shows schematically how the rat and fox may pass on the disease to one another and the sequence might well be : fox–wild rat–home rat–pig–man.

H. Harold Scott.

DEFICIENCY DISEASES.

CLARKE, B. L. W. **Deficiency Diseases.** *Med. J. Australia.* 1946, Aug. 3, v. 2, No. 5, 162–6.

This paper is a brief survey of the effects of malnutrition that occurred among Australian prisoners-of-war in Singapore. Among the conditions mentioned are beriberi, nutritional oedema, the "painful feet" syndrome, scrotal dermatitis, pellagrous skin lesions, and ulceration of the skin after injury. Of particular interest is a syndrome which appeared to be an allergic reaction to a certain type of bean of the calabar variety. The initial symptom was burning or pricking of the skin, followed by oedema, which rapidly increased. Later the skin began to peel, leaving a raw bleeding surface. A most remarkable feature was severe agranulocytosis, the leucocyte count often falling to a few hundred cells per cmm. Other manifestations were swelling of the lips and tongue, ulceration of the buccal mucosae, and fissures at the corners of the mouth and round the anus. Many patients after recovery were left with patchy areas of depigmentation of the skin. No details are given of the mortality of this disease, nor of the response to different forms of treatment. *J. C. Waterlow.*

LANG, W. R. **Vitamin B Deficiency in Ex-Prisoners of War from Japan.** *New Zealand Med. J.* 1946, Aug., v. 45, No. 248, 296–307. [15 refs.]

"An account is given of 85 servicemen who had been interned in Japan and who came to New Zealand suffering from beri-beri, pellagra, worm infestation, amoebiasis and other affections. Their state on admission, treatment and general management and progress are described, and three illustrative case histories reported. Attention is given particularly to Vitamin B deficiencies, and these are discussed and some conclusions drawn from the present series."

SIMONS, R. D. G. P. Pellagrosis (Morbus Strachan-Scotti of Dermoberiberi Castellani) onder Krijgsgevangenen op Java en Sumatra. [**Pellagrosis in Prisoners of War in Java and Sumatra.**] Reprinted from *Nederl. Tijdschr. v. Geneesk.* 1946, July 20, v. 90, No. 29, 843–7. English summary.

"Among a great number of Netherlands and British prisoners of war in Java and Sumatra vitamin deficiency was observed consisting of pellagra and some other symptoms which occurred simultaneously. STRACHAN, SCOTT and CASTELLANI previously mentioned syndromes consisting of similar symptoms.

"If one should wish to reserve the term of pellagra for the triad of KNOWLES (diarrhea, dermatosis and depression or dementia) another term is required *e.g.* pellagrosis, which includes the obsolete 'pellagra', Morbus CASTELLANI (dermoberiberi) and the disease of STRACHAN and SCOTT. The observed symptoms have been enumerated in this article."

SCHMIDT, V. Pantotensyre. [**Pantothenic Acid.**] *Nordisk. Med.* 1946, Nov. 1, v. 32, No. 44, 2492–4. [Summary in English by the author.]

"A summary is given of the occurrence, chemistry, and physiology of pantothenic acid. Report is given of known pantoten deficiency symptoms in animals, compared to investigations into the occurrence, effect, and characteristics of pantoten in certain diseases in man. Special mention is made of GOPALAN's statements regarding the effect of pantothenic acid in the 'burning feet' syndrome. Finally, a review is given of pantothenic acid-antivitamin research."

GELFAND, M. **Kwashiorkor.** *Clin. Proc.* Cape Town. 1946, June, v. 5, No. 4, 135–53, 2 figs. [18 refs.]

In recent years increasingly frequent descriptions have appeared, from different parts of Africa, of the disease known as "kwashiorkor", or infantile pellagra—TROWELL [this *Bulletin*, 1941, v. 38, 722]; GILLMAN & GILLMAN [*ibid.*, 1946, v. 43, 59, 365]; HUGHES [*ibid.*, 766]; RUSSELL [*ibid.*, 1947, v. 44, 118]. The cases reported here from Southern Rhodesia were typical examples of the syndrome. All were infants between one and two years old, with crazy-pavement dermatosis, fissures at the mucocutaneous junctions, and depigmentation of the skin and hair. Wasting was severe; oedema was present in three-quarters of the cases, and the liver was usually enlarged. Steatorrheoa was not always found, but four cases examined radiologically showed gross segmentation of barium in the jejunum, BROWN & TROWELL [this *Bulletin*, 1945, v. 42, 306]. At post-mortem there was severe fatty infiltration of the liver; subcutaneous fat was usually absent. Dried stomach was found to be of no value in treatment; six out of seven patients who received this substance died.

The author maintains that kwashiorkor is not a nutritional disease. His argument may be summarized as follows: the history is too short—usually less than a month—and the maximal incidence is just at the time of year when the diet of the native is at its best. Mild cases, which are easily cured by dietary measures, are really cases of acute gastro-enteritis. Finally, in 9 out of 12 cases, for which a dietary history was obtained in detail, there was no evidence of inadequate feeding.

The fatty change in the liver is considered to be the primary feature of the disease: the other manifestations are secondary to interference with the metabolism and storage of vitamins and other nutrients. The liver lesion is ascribed to the action of toxins, and examples are given of cases not related to malnutrition, in which a similar degree of fatty infiltration was observed—namely, two infants dying after severe burns, and one dying of miliary tuberculosis.

[This paper contains two points of particular interest: the first is the failure of dried stomach as a method of treatment; the second is the suggestion that kwashiorkor is not a nutritional disease.

GILLMAN & GILLMAN (1944) introduced the use of dried stomach in the treatment of infantile pellagra. They claimed that it acted as a specific cure (1945b), and in a large series of cases found a lower mortality with this than with any other form of treatment (1946). Favourable results were also reported by TROWELL & MUWAZI (this *Bulletin*, 1946, v. 43, 363). The failure of dried stomach in Gelfand's cases cannot be attributed to inadequate dosage: 6 drachms daily of either "Pepsac" (Boots) or of the preparation made by Paines and Byrne were given for several weeks, or until death occurred. GILLMAN & GILLMAN (this *Bulletin*, 1947, v. 44, 118) using "Ventriculin" (Parke Davis), obtained a good response with a much smaller dose (10 gm. daily for 5 days). This form of treatment is still in the experimental stage, and therefore differences in the preparation used must be taken into account in assessing the contradictory results.

Until the active factor in dried stomach, if such there be, is isolated, the aetiology of kwashiorkor remains in doubt. It must be admitted that the evidence that it is a deficiency disease is by no means complete. This evidence is derived from observations of two kinds: the resemblance of some of the features of the syndrome to those of known deficiency states, and the general conditions under which the disease is found. There have, however, been few detailed descriptions of the dietary background, and no accurate records of

food intake, either in the patients themselves or in members of the same population. In spite of these gaps in our knowledge, the weight of opinion, in all parts of the world in which the disease occurs, is that it is the result of dietary deficiency. The evidence which Gelfand brings against this view is slender. A short history is of little significance, because it refers only to the duration of frank and obvious symptoms, which may have been preceded by a longer period of under-nutrition. The prodromal symptoms and signs—irritability, failure to thrive, etc.—are so common among infants of a generally malnourished population that they excite no comment. This point has been emphasized by TROWELL (this *Bulletin*, 1946, v. 43, 1062.)

Since no details of the native diet are given, it is not possible to assess the significance of the seasonal incidence. PIERAERTS (this *Bulletin*, above, p. 225, and also 1942, v. 39, 99, and 1943, v. 40, 406) showed clearly that the similar, if not identical, disease "diboba" reaches epidemic proportions at the time of year when the diet is at its worst, consisting of manioc alone, with no cereal, greenstuffs, or animal food.

The statement that mild cases which respond to any form of treatment are really cases of acute gastro-enteritis raises the question "what are the diagnostic criteria of kwashiorkor ?" In an earlier passage of this paper it was stated that cases without oedema are to be differentiated from gastro-enteritis by the presence of depigmentation. The borderline between kwashiorkor, marasmus and nutritional oedema of infants associated with gastro-enteritis, is not clearly defined. Until the aetiology is better understood the definition of what is and what is not kwashiorkor remains a matter of convention.]

J. C. Waterlow.

HYNES, M., ISHAQ, M. & MORRIS, T. L. **Serum-Protein Level of Indian Soldiers.** *Lancet.* 1946, Oct. 26, 590–94, 2 figs.

When the copper sulphate method was used to estimate serum proteins, it was found that the moderate exercise of marching one mile raised the average serum-protein level of Indian soldiers by 0·3 gm. per 100 ml., and in some individuals by thrice this amount. After 30 minutes' rest the protein fell to a stable resting level. Violent exercise for 5 minutes raised the average serum-protein level by 0·75 gm. ; the resting level was not reached until an hour after. These findings emphasize the importance of taking blood for serum-protein estimations after a strictly standardized period of rest. No difference was found in the degree of change with exercise in recruits and trained men : the values in recruits were however higher than in trained men.

Similar alterations with exercise were found also in the level of the haemoglobin and in the volume of the packed red cells. Gentle exercise led to average increases of 0·4 gm. haemoglobin per 100 ml. blood, and 1 per cent. in the packed cell volume. Violent exercise gave average increases of 0·9 gm. Hb. and 4 per cent. packed cell volume. A discussion is given of the possible significance of these findings, which raise many interesting questions without providing the answers.

H. E. Harding.

SPRUE.

BLACK, D. A. K. **Salt Deficiency in Sprue.** *Lancet.* 1946, Nov. 9, 671–5.

In both tropical and non-tropical sprue blood-pressure is lower than normal. Though a fall in blood-pressure is more common in long-standing cases, in 41 soldiers with sprue who had been in India 4 years or less, four had a systolic

blood-pressure of less than 100 mm. Hg and a diastolic of less than 65 mm. Some of these showed signs of peripheral circulatory failure.

The ten patients investigated were selected from several hundreds who passed through the hospital in 15 months. The basis of selection was low-pressure with asthenia. The pulse was thin and rapid. The muscles and subcutaneous tissues were flaccid, the skin wrinkled.

Seven of the patients had a *plasma volume* of less than 2·5 litres ; two of less than 2·0 litres and five of less than 45 mgm./kg. The haematocrit readings lay mostly between 40 and 46 per cent. The *serum-sodium* values were uniformly low, ranging from 258–320 mgm./100 ml. The *serum-potassium* in seven patients did not exceed upper limit of normal. The *serum-chlorides* were also low. All this indicated that hypotension and circulatory failure are associated with low serum-sodium and serum-chloride levels, less constantly with a low plasma volume.

In later patients of the series, treatment with salts, either by mouth or intravenously, was followed by disappearance of circulatory collapse and serum-sodium rather slowly returned to normal levels.

Blood estimations showed a low serum-sodium level which rose rapidly when salt was added to the diet. A balance experiment on a typical patient showed abnormal loss of sodium, and to a less extent of chloride in the faeces : in the urine, sodium was rigidly conserved while chloride was excreted in less than normal amounts.

The clinical and laboratory findings suggested that dehydration was due to salt deficiency. The comparative frequency of this as a complication of tropical sprue does not seem to have been appreciated for when the patient is put on a high intake of salt, sodium and chloride were both retained and the serum-chloride and serum-sodium rose to normal levels. The blood-pressure rose and clinical signs of dehydration disappeared, though the abnormal loss of fat in the stools was not affected.

Loss of electrolyte in copious watery stools is considered to be the main cause of the salt deficiency, though diminished intake of salt in anorexic patients may also be a factor.

The results do not suggest that adrenal insufficiency can be considered, as the serum-potassium was not increased. Treatment by increasing the salt intake to 15 gm. a day corrects the dehydration in a few days. *P. Manson-Bahr.*

VENOMS AND ANTIVENENES.

KHAN, F. **Snake-Bite.** *J. Indian Med. Ass.* 1946, June & July, v. 15, Nos. 9 & 10, 303–7 ; 343–8.

This is an elementary lecture treating first of snake-bite in general terms and then describing the 18 snakes of the Hyderabad Deccan, each in a few words ; four only of these are poisonous, namely *V. russelli* (daboia), *Echis carinatus* (phoorsa), the Cobra (*N.naja* and *tripudians*) and *Bungarus caeruleus* (krait). The mechanism of biting and injection of venom and its action are then spoken of (even to mentioning tips or mnemonics for diagnosis and symptoms) and treatment by antivenenes, with a copy of the instruction sent out by the Director General of the Kasauli Research Institute. Need is stressed for early administration of the antivenene and the warning that it must be given only by a medical man. [No mention is made of the first aid treatment by carbolic soap emulsion to tide over the dangerous interval between infliction of the bite and the arrival of the doctor. See this *Bulletin*, 1946, v. 43, 478.]

H. Harold Scott.

BOQUET, P., GIRARD, O. & CORVAZIER, R. Note sur la préparation des sérums antivenimeux (anti *Vipera aspis*, *Cerastes cornutus* et *Bitis arietans*). [**Preparation of Antivenenes to the Venoms of** *Vipera aspis*, *Cerastes cornutus* **and** *Bitis arietans*.] *Ann. Inst. Pasteur.* 1946, July–Aug., v. 72, Nos. 7/8, 660–62.

After describing briefly Calmette's original method of preparing antivenenes by injecting graded doses of the venom with calcium hypochlorite subcutaneously into horses the authors state that, wishing to replenish their stock, they found that they had very little venom left. By using anavenoms they obtain much more rapid immunization with less material. Ten per cent. solutions of the venoms are centrifuged at 12,000 r.p.m. for 20 minutes to remove bacteria; then 5 per 1,000 formol is added and horses are inoculated with increasing doses twice weekly. When 1 cc. of the serum neutralizes 1 mgm. of the venom the horses are bled and the serum obtained for use.

Under the older method, for *V. aspis* antivenene a total of 577 mgm. of venom was needed and 8–11 months requisite for preparing the antivenene. For *Cerastes cornutus* 730 mgm. were needed and immunization to the degree required took 5 months and 11 days. For *Bitis arietans* 843 mgm. spread over 9 months. Under the new, anavenom, method a satisfactory *V. aspis* antivenene was obtained in 2½ months and the total injected was 360 mgm.; for *C. cornutus* 482 mgm. were injected and the antivenene was obtained in 2 months 22 days; for *B. arietans* 391 mgm. injected over a period of 5 months.

The new method using anavenom is, therefore, more rapid in attaining the desired strength of antivenene and a smaller amount of venom is required.

H. Harold Scott.

HAZRA, A. K., LAHIRI, D. C. & SOKHEY, S. S. **On the Standardisation of Haffkine Institute Polyvalent Anti-Snake-Venom Serum against the Venoms of the Four Common Indian Snakes (Cobra, Common Krait, Russell's Viper and Saw-Scaled Viper).** *Bull. Health Organisation.* (League of Nations.) 1945/46, v. 12, No. 3, 384–9, 4 diagrams.

DERMATOLOGY AND FUNGUS DISEASES.

YOUNG, D. C. **Secondary Infection of Dermatophytosis. Report of a Case.** *U.S. Nav. Med. Bull.* 1946, Oct., v. 46, No. 10, 1604–5.

CURY, A. Ação fungistática da tirotricina "in vitro". [**Fungistatic Action of Tyrothricin** *in vitro*.] *Brasil-Medico.* 1946, Aug. 17, 24 & 31, v. 60, Nos. 33, 34 & 35, 273–6. English summary.

Tyrothricin is an antibiotic substance obtained from a sporing aerobe, *B. brevis*, and has a bactericidal and bacteriostatic action on pneumococci, streptococci and staphylococci. Later, it was isolated from the culture medium and was shown to consist of two substances, gramicidin and tyrocidin. Many papers have been published relating its antibacterial action, but not much on its antifungal properties. The author has tested it in dilutions ranging from 1 : 2,000 to 1 : 128,000 on 32 species of fungus, some pathogenic, others non-pathogenic. The detailed results are presented in a table, but may be summed up as follows: On five (among them, *Aspergillus fumigatus* and *Hormodendron langeroni*) it had no action at all; on ten others the effect was to inhibit growth at 1 : 2,000 but not at 1 : 4,000 (among these were *Trichophyton rubrum*, *Sporotrichum schencki*, *Phialophora pedrosoi* and *P. verrucosa*); four others were inhibited at 1 : 4,000 but not at 1 : 8,000 (including *Coccidioides immitis* and

Achorion schönleini) ; another five at 1 : 8,000 (including *Actinomyces bovis*) ; *Gilchristia* (*Blastomyces*) *dermatitidis* at 1 : 32,000 ; and *Histoplasma capsulatum* at 1 : 128,000.

Tyrothricin is thus seen to have no selective action on any particular group of fungi, but these results warrant a trial of it in some of the cutaneous mycoses of man and animals. *H. Harold Scott.*

GONÇALVES, A. P. Estudo das concentrações sanguíneas das sulfonamidas no decurso do tratamento da blastomicose brasileira. [**The Concentration of Sulphonamide Drugs in the Blood in the Treatment of Blastomycosis in Brazil.**] *Hospital.* Rio de Janeiro. 1946, June, v. 29, No. 6, 875–81.

According to modern ideas, for successful treatment by members of the sulphonamide group a certain concentration of the drug in the blood must be maintained, the degree of concentration differing according to the drug used and the nature of the infecting organism. The author has investigated from this point of view the actions of sulphathiazol, sulphapyridine, sulphadiazine and sulphamerazine.

The numbers of patients treated with each drug were very small, 9 with the first, 1 with the second, 4 with the third and 2 with the last. [In no case is the nature of the mycosis, or the site involved or the extent of disease mentioned.] American investigators, says the author, aver that it is necessary to maintain a blood concentration of 5–15 mgm. of the drug per cent. ; Brazilian mycosis rarely needs more than 5 mgm. per cent. The author found that this amount was sufficient for sulphamerazine and sulphadiazine, and a little less for sulphathiazole. The two former have the additional advantage that the concentration can be maintained when longer intervals are allowed to elapse between the doses. If the lesion is slow to clear up, it is necessary to ascertain first if the patient is keeping up the treatment before going on to increase the dosage. This warning is given because many patients are reluctant to persevere with the treatment. *H. Harold Scott.*

RAKOFSKY, M. & KNICKERBOCKER, T. W. **Roentgenological Manifestations of Primary Pulmonary Coccidioidomycosis.** *Amer. J. Roentgenol. & Radium Therapy.* 1946, Aug., v. 56, No. 2, 141–55, 10 figs. [13 refs.]

This study is based on observation of 60 cases of primary coccidioidomycosis, 12 of them severe, with extensive lung involvement. By "primary coccidioidomycosis" is implied the mild bronchopneumonia cases with cough, pain in the chest, fever and erythema nodosum, recovering completely in 3–6 weeks. [The secondary or chronic stage, with cutaneous and bony lesions and widespread involvement, has a high fatality rate, approaching 50 per cent.] In the dark-skinned races, among the members of which natural immunity is low, the course may be of a fulminating type from the first with rapid dissemination of lesions.

The authors classify the X-ray findings as follows : (1) *Nodular lesions,* resembling tuberculous deposits ; these may be single or multiple and on one side or both ; found in 22 per cent. of the authors' series. (2) *Peribronchial infiltration,* which may be associated with nodular lesions and enlargement of the hilar glands, 22·5 per cent. (3) *Confluent consolidations,* small or large, even to lobar involvement, 20 per cent. (4) *Enlargement of hilar glands,* some with the peribronchial infiltration referred to above, less often in a pure form, 24·5 per cent. together, 16·5 and 8 per cent. respectively. (5) *Involvement of pleura,* with dry, adhesive pleurisy or with effusion, 5 per cent (6). *Cavity formation,* 5 per cent. ; it may be surrounded by pneumonic consolidation.

When less well known, this was, excusably, regarded as tuberculous. (7) *Bilateral nodular dissemination*, more common in negroes, 20 per cent. Though widespread through the parenchyma of both lungs, the distribution appears to be rather a local dissemination.

Five cases are described in detail, with reproduction of the X-ray pictures of the lungs and photographs of the lung consolidation. Four were in negroes, one ended fatally, and one in a Mexican, also fatal. The negro who died had a widespread fulminating disease supervening on a severe primary coccidioidal infection, the Mexican was suffering from combined coccidioidomycosis and tuberculosis. *H. Harold Scott.*

ARNOLD, W. T. & LEVY, M. D. **Coccidioidomycosis treated with Penicillin. Case Report.** *Southern Med. J.* 1946, Aug., v. 39, No. 8, 609–13, 2 figs.

This case of coccidioidomycosis presented difficulties to diagnosis. The patient, a male negro aged 32, suffered an acute illness with low-grade fever, cough with haemoptysis and night sweats, and dull substernal pain. Shortly afterwards, an X-ray examination showed a solid mass in the region of the hilum of the left lung, which was thought to be a bronchogenic carcinoma. Examination of an excised supraclavicular lymph node, however, led to the diagnosis of tuberculous lymphadenitis, but this diagnosis was changed to Hodgkin's disease when a general enlargement of the mediastinal glands was discovered. At this stage some improvement was effected by X-ray therapy, but subsequently a subcutaneous granuloma developed on the back, broke down and ulcerated. Biopsy material from this lesion showed *Coccidioides immitis*. On re-examination, the supposed tuberculous lymph node was also found to be coccidioidal. The patient died one year after the onset of signs of meningitis. Penicillin treatment amounting to 3,200,000 units by the intramuscular route and 75,000 units intrathecally had proved ineffective. [There is nothing in the report of the case to show that a coincident tuberculous infection could be excluded.] *J. T. Duncan.*

TROPICAL ULCER.

SMYTH, E. A. **The Treatment of Tropical Ulcer.** *J. Roy. Army Med. Corps.* 1946, Sept., v. 87, No. 3, 141–2.

The author treated 637 patients suffering from tropical ulcer in a P.O.W. camp hospital in Siam. In the absence of adequate therapeutic facilities, he was forced to amputate the leg in eight cases, so rapid and extreme was the destruction.

Later, he employed a method based on the employment (after preliminary removal of pus by general cleansing methods) of pure carbolic acid, followed by orthodox dressings and gradually reduced in strength until two daily applications of 1 in 13 carbolic are applied.

In order to economize in carbolic acid a mixture of 2½ per cent. carbolic in 1 per cent. perchloride of mercury was substituted for the 1 in 13 carbolic with equal success, but with slight pain to the patient.

No signs of carbolic acid poisoning appeared. The strengths and daily applications of carbolic acid are given in the text.

The author believes that some of the amputations could have been avoided if this treatment had been instituted earlier. *H. J. O'D. Burke-Gaffney.*

MISCELLANEOUS DISEASES.

DAVIES, J. N. P. **An Accessory Liver in an African.** [Memoranda.] *Brit. Med. J.* 1946, Nov. 16, 736–7.

SOUBIGOU, X. A propos de funiculite tropicale. [**Tropical Funiculitis.**] *Bull. Soc. Path. Exot.* 1946, v. 39, Nos. 7/8, 287–9.

BENHAMOU, E., NOUCHY & SEBAH, P. Noma et pénicilline. [**Penicillin in the Treatment of Cancrum Oris.**] *Algérie Méd.* 1946, May–June, No. 3, 264–8.

Five cases are described. One, a man of 32 years, in whom cancrum oris complicated an attack of measles. The blood examination ruled out agranulocytosis. All the usual treatments—mouth washes, silver nitrate, Vitascorbol, sulphonamides, etc.—were tried in vain and he was given 100,000 units of penicillin daily, administered every 3 hours, for 12 days. Improvement, though gradual, was steady and cure was obtained in 15 days.

The second patient, a woman with typhoid fever [age not stated], 4 days after admission to hospital on the 20th day of her illness, developed noma, and two days later penicillin intravenously was started, 20,000 units every 3 hours. Improvement was observed " after the third injection (160,000 units) " [says the author, but 3 injections of 20,000 units would be only 60,000]. She left hospital, cured, a month after her admission. In three other cases of typhoid, in a boy of 12 years and two women, of 17 and 38 years, equally good results were obtained [but the last patient died later after a surgical operation the nature of which is not mentioned]. References to the literature are given in which cure of noma and other buccal conditions, *e.g.* Vincent's angina are recorded and the author found *B. fusiformis* in two of the five cases he reports in this paper and he states that he has put these on record " not only to add to the reports of the beneficial effects of penicillin in noma, but to stress also the fact that the fusiform bacillus is often associated with these gangrenous ulcers and that disappearance of these organisms is soon followed by cure."

H. Harold Scott.

TUPAS, A. V. & JONGCO, A. P. **Cancrum Oris : Observations on its Incidence and Treatment.** *J. Philippine Med. Ass.* 1946, Apr., v. 22, No. 4, 153–7. [15 refs.]

" 1. Fifteen cases of cancrum oris admitted and treated in the Pediatrics Department of the Philippine General Hospital from April 4, 1945, to April 5, 1946, were presented.

" 2. The incidence of noma in the Philippines, before, during, and after the second world war was discussed.

" 3. A reduction of the mortality rate from 70–100 per cent. to 6·67 per cent. with the use of sulfa drugs and penicillin was reported.

" 4. Other reports on the incidence, mortality, and treatment of cancrum oris were briefly reviewed and compared with our findings."

CEYLON HEALTH NEWS. 1945, Oct.–Dec., v. 12, No. 2, 11–12. **Manioc Poisoning.**

In the present food crisis, the cultivation and consumption of manioc is increasing and is likely to continue to increase, and cases of poisoning have already occurred in Ceylon.

The present paper is intended to guide the population in the safe use of manioc and to aid doctors in investigating suspected poisoning cases thoroughly.

Manioc contains a cyanogenetic glucoside harmless in itself; but when the root is bruised or damaged an enzyme is set free which breaks up the glucoside and liberates the hydrocyanic acid.

The glucoside is concentrated in the outer layers of the roots, and chemical analyses show that whilst the peel contains an average of 0·1 per cent. of HCN, the rest of the root only contains 0·003 per cent., the purpose of the glucoside being to serve as a potential protection of the root from pests.

In the preparation of manioc, the following precautions are necessary :—

1. It should not be bruised or crushed and damaged roots should be discarded.
2. The roots should be fresh, and not be exposed to sunlight for long.
3. For cooking, the outer rind should be peeled off, the roots quickly washed, and the pot only half filled with the peeled roots.
4. The water level should be above the surface of the yam, so that steam does not condense on the exposed manioc.
5. The vessel should not be covered, so that any remaining poison may escape with the steam.
6. The water used for boiling the manioc should be thrown away.

In treating manioc poison, uncooked fresh plant materials, such as ginger, should be avoided, since their enzymes would liberate the HCN from the glucoside. A mixture containing ferrous and ferric salts with a little bicarbonate of soda should be given. Other adjuvants to treatment are (1) stomach wash-out; (2) sodium thiosulphate solution intravenously; (3) care of the general condition of the patient.

The investigation of a suspected case of manioc poisoning should take account of the history of the meal and the number of persons taking it; the source and condition of the manioc, especially whether it was fresh or bruised; the method of cooking; whether the root was peeled, and the quantity of water used and its disposal. *H. J. O'D. Burke-Gaffney.*

GREVAL, S. D. S. & BHADURI, P. N. **Poisonous Foodgrain : Wheat mixed with** *Lolium temulentum. Indian Med. Gaz.* 1946, Aug., v. 81, No. 8, 294–6, 4 figs. on 1 pl. [18 refs.]

In the period October 1942–November 1945, some 450 persons in Aden suffered from *loliismus*; the symptoms were typical and there were no fatal cases; recovery of consciousness took place in 3–10 hours and all were able to return to work in 3 days. In Arabia, the weed is usually separated from the wheat before reaping-time, or, as in Abyssinia, the wheat is separated by sieving or by winnowing, but this was not done in Aden. The actual poisoning is now known to be due to a contaminating fungus between the seed-coat and the endosperm, living symbiotically in the grains—a type of smut fungus. The author describes the weed and its distribution, facts with which readers of this *Bulletin* are well acquainted. Two photographs show well the resemblances and differences between the grains of wheat and those of *Lolium temulentum.*

H. Harold Scott.

MANCEAUX, A. & SUSINI, R. Les crises nerveuses dans l'armée (étude portant sur 1,100 cas). [**A Study of Nervous Disturbances in 1,100 Troops in Algeria.**] *Algérie Méd.* 1946, July–Aug., No. 4, 331–4.

GENERAL PROTOZOOLOGY.

SANTOS ZETINA, F. El vital problema sanitario de la zona Henequenera. [**Sanitary Problems in the Henequenera District (of Yucatán).**] *Rev. Med. Yucatán.* 1946, Aug. 31, v. 23, No. 12, 523–6.

During the year 1945 the following numbers of cases of infections and infestations have been recorded in the zone in question. *Intestinal parasites*: *E. histolytica, Balantidium coli, L. intestinalis, A. lumbricoides, Trichuris trichiura, Enterobius vermicularis* and hookworm, 72,072. The percentages are given of 10,920 at one hospital; these were *Trichuris* 63·17, *Ascaris* 40·9, *Trichomonas* 28·6, *Lamblia intestinalis* 24·1, *Entamoeba histolytica* 15·3, *Taenia* sp. 3·31, *Tetramitus mesnili* 1·2, *Necator americanus* 0·8. It is "conclusively affirmed" that 90 per cent. of the children in Yucatán harbour parasites.

During the year, 15,391 cases of malaria were recorded [but no details as regards type], cases of syphilis numbered 5,739, of tuberculosis 3,206 and of enteric fevers 1,577. [The population of the district is not mentioned, so the actual degree of prevalence cannot be estimated and the figures in consequence are not very informative.] *H. Harold Scott.*

WATSON, J. M. **The Bionomics of Coprophilic Protozoa.** *Biol. Reviews.* 1946, July, v. 21, No. 3, 121–39. [Numerous refs.]

GENERAL ENTOMOLOGY.

MELLANBY, K. **Man's Reaction to Mosquito Bites.** [Correspondence.] *Nature.* 1946, Oct. 19, 554.

People react differently to insect bites, and repeated exposure may alter a given person's reactions. In order to pursue these factors further, studies were made on human volunteers, who had never travelled outside Britain, and who were exposed experimentally at different periods to the bites of *Aëdes aegypti* and *Anopheles maculipennis atroparvus.*

Twenty-five volunteers all gave a similar reaction. At first there was no immediate reaction following a bite by *A. aegypti* (other than a tiny spot) and no itching. A marked delayed reaction occurred usually between 20 and 24 hours, in the form of a red patch about 3 cm. in diameter surrounding the bite, with a definite weal in the central one-third. The itching and other manifestations waxed and waned for several days.

After repeated biting by *A. aegypti* over a period of a month, the resultant reaction was quite different. An immediate reaction developed, now taking the form of a weal with an area of erythema around it, and with itching of the skin. These manifestations disappeared within 2 hours, but the former delayed reaction ensued within 20 to 24 hours as before. After further exposure, the reaction was further modified by the gradual diminution and eventual disappearance of the delayed reaction. In other persons repeatedly exposed to thousands of bites by *A. aegypti*, it was observed that the immediate reaction also disappeared.

The author thus tabulates man's reactions to *Aëdes aegypti* bites as observed by him, in serial stages after further exposure :—

	Immediate Reaction	Delayed Reaction
Stage I	—	+
,, II	+	+
,, III	+	—
,, IV	—	—

It is suggested that the reactions are distinct and are caused by different antigens in the mosquito's saliva.

Similar, though not identical, results were obtained with *A. maculipennis atroparvus*. The phenomena of sensitization and immunity in the reactions appear to be specific: for example, one person may give a stage I reaction to *Anopheles* and a stage II reaction to *Aëdes* simultaneously.

Investigations, still being pursued, appear to indicate that other species of biting insects fit into the scheme, with modifications: and that most people react similarly to the same degree of exposure, though in some cases hypersensitivity and severe allergy occur. *H. J. O'D. Burke-Gaffney.*

HOLLENBECK, A. H. **A Practical Method for Mass Production and Transfer of** *Xenopsylla cheopis*. *J. Parasitology.* 1946, Oct., v. 32, No. 5, 463–4, 1 fig.

NÁJERA, L. **The Ecology of Sandflies at the Larval Stage and the Epidemiology of the Diseases transmitted by them.** *Bull. Health Organisation.* (League of Nations.) 1945/46, v. 12, No. 3, 394–406, 6 figs. & 1 plan. [29 refs.]

This contains much the same information as the paper by the same author, abstracted in this *Bulletin*, 1946, v. 43, 832.

COUDERT, J. & BAUD, C. Procédé de montage des échantillons parasitologiques dans les verres synthétiques. [**Mounting Parasitological Specimens in Transparent Plastics.**] *Ann. Parasit. Humaine et Comparée.* 1946, v. 21, Nos. 3/4, 177–82, 3 figs.

The authors wish to preserve teaching material, such as whole insects, in such a way that students can examine and handle it but without breaking the specimen. They do this by embedding in a block of a transparent plastic.

The authors prefer to use methyl methacrylate, but have worked with vinyl acetate and styrolene. Their general method is to distil a quantity of the monomere, and soak the dehydrated specimen in it. Some of the monomere is then polymerized by heat in the presence of a catalyst, and as it thickens is poured into a mould, the specimen being transferred to it at the same time. Polymerization is completed in a stove. When the moulded block is hard it is rubbed down and polished with abrasives.

Small dissections, and such soft animals as worms, can be embedded, dehydration being very slow to avoid shrinkage. *P. A. Buxton.*

GARNHAM, P. C. C. **The Efficacy of Insecticidal Sprays in Aircraft.** *East African Med. J.* 1946, Sept., v. 23, No. 9, 272–7.

Routine disinfestation of aircraft is now carried out practically everywhere in the tropics. The method used at Kisumu in East Africa involves the use of aerograph pressure sprays with pyrethrum preparation content, the quantity of solution sprayed in the closed aircraft is at the rate of approximately 40 ccs. per 1,000 cu. ft., and time of exposure ten minutes. [The pyrethrin content of the preparation is not quoted; Shelltox and Deskito were among those used and presumably approximated 2 per cent. pyrethrin content after dilution.]

Routine testing of the efficacy of this treatment is effected by the results of exposure to the spray of three female *Aëdes aegypti*, and three *Taeniorhynchus uniformis* contained in a mosquito cage, a three inch cube in size. Three such cages are used and placed at strategic positions within the aircraft. An effective spraying should result in the stunning of all mosquitoes in five minutes, and no survivals after fifteen hours, the cages having been removed in a Barraud's box after ten minutes exposure.

The efficacy of such disinfestation in inaccessible places within the aircraft was also investigated and the conclusion was that a higher dosage, namely 46 cc. per 1,000 cu. ft., was necessary to ensure killing all mosquitoes hidden in remote corners.

Experiments conducted to determine the degree of protection to mosquitoes ensured by coats, wraps, etc., accompanying the passengers in the aircraft, showed that even a thin covering is apparently sufficient to protect caged mosquitoes from heavy doses of powerful insecticide. This observation led to further experiments in the laboratory in which mosquitoes were placed inside the sleeves of raincoats and the raincoats exposed to various dosages of insecticide. Using the freon bomb dosages of seventeen seconds per 1,000 cu. ft. were ineffective ; four times this concentration killed most of the mosquitoes ; the usual doses of this insecticide in an aircraft would be four to six seconds per 1,000 cu. ft. ; there did not appear to be any tendency on the part of mosquitoes to leave the sleeve because of irritation by the mere presence of the insecticide.

The author concludes that all parts of the aircraft are accessible to insecticides if used in sufficient concentration, with the provision that particular care must be taken in regard to the possibility of mosquitoes being protected by clothing. He recommends spraying of the aircraft while in flight or just before departure, the latter being less satisfactory.

[In practice, effective results must necessarily depend on the efficiency of the staff, the whole process being subject to inspection by the local health authority.] *R. Ford Tredre.*

STEWARD, J. S. **Application of "Gammexane" to Arthropods of Veterinary Importance.** *Nature.* 1946, Nov. 2, 636–7.

GUYANE FRANÇAISE : RAPPORT SUR LE FONCTIONNEMENT TECHNIQUE DE L'INSTITUT PASTEUR DE LA GUYANE FRANÇAISE ET DU TERRITOIRE DE L'ININI PENDANT L'ANNÉE 1945 [FLOCH, H., Director]. (Publication No. 125. 1946. Cayenne.) pp. 114–33. [12 refs.] Entomologie. [**Entomology**] ; pp. 133–4. Acariens. [**Acaridae**].

These notes, though published under the name of the Institute are presumably contributed by the entomologist, E. Abonnenc. They cover a wide range of subjects, mosquitoes, *Phlebotomus*, *Simulium*, urticating moths, and Ixodid ticks. The information is difficult to summarize : much of it is published probably more fully in the Institute's publications : more than twenty of these, published separately, were issued in 1945. *P. A. Buxton.*

GUYANE FRANÇAISE : RAPPORT SUR LE FONCTIONNEMENT TECHNIQUE DE L'INSTITUT PASTEUR DE LA GUYANE FRANÇAISE ET DU TERRITOIRE DE L'ININI PENDANT L'ANNÉE 1945 [FLOCH, H., Director]. (Publication No. 125. 1946. Cayenne.) pp. 102–12. [11 refs.] Insecticides végétaux en Guyane. [**Vegetable Insecticides in Guiana.**]

The infusions of various plants growing in French Guiana were tested for toxicity to larvae of Anopheline and Culicine mosquitoes, to the larvivorous

fish, *Poecilia vivipara*, and to several fresh water snails (elsewhere carriers of bilharzia). Of the plants tested, the fruits of *Sapindus saponaria* Aublet, leaves and shoots of *Baillieria aspera* Aublet and seeds of the avocado pear, *Persea gratissima* Gaertner had some insecticidal action, but definitely less than that of derris containing 5 per cent. rotenone. These plants were used as fish poisons and were toxic to *Poecilia*. The seeds of the fruits of *Mammea americana* L. (Gutiferae) seemed more likely to have practical value, for they gave an extract nearly as toxic as the derris and less poisonous to fish.

The seeds of *Sapindus saponaria* had a definite toxic action on fresh-water snails probably because of their high saponin content.

DDT powder was more toxic than rotenone to mosquito larvae though it was somewhat slower in action ; it had little or no effect on the mollusca.

J. R. Busvine.

LABORATORY PROCEDURES.

KAUMP, D. H. **Laboratory Tests in General Practice.** *J. Amer. Med. Ass.* 1946, Oct. 5, v. 132, No. 5, 253–8. [Refs. in footnotes.]

SINGER, R. **A Note on Leishman Staining.** [Correspondence.] *Clin. Proc.* Cape Town. 1946, June, v. 5, No. 4, 183–4.

The author was unable to obtain acetone-free methyl alcohol during the War and he therefore used ordinary absolute alcohol in a modification of the self-buffering solution described by WITLIN [this *Bulletin*, 1945, v. 42, 232]. The cost of the absolute alcohol was considerably less than that of methyl alcohol of the kind required.

The solution was prepared by dissolving 120 mgm. of sodium acetate in 100 cc. of absolute alcohol, and adding to this solution 0·4 cc. of a solution of 0·1 cc. glacial acetic acid in 100 cc. absolute alcohol. This is the same prescription as that of Witlin except that (*a*) absolute alcohol replaces methyl alcohol throughout, (*b*) Witlin used a 1·0 per cent. solution of glacial acetic acid.

[The author states that, in his modification, " the total amount of acetic acid in 100 cc. of sodium acetate-acetic-acid absolute-alcohol-solution is 0·004 cc." If 0·1 per cent. glacial acetic acid was used originally, this total should read 0·0004 cc. Witlin, in his original paper, used 0·1 cc. of glacial acetic acid in ten, not one hundred, cc. of methyl alcohol, *i.e.* a 1 per cent. solution, and stated, correctly, that the total amount of acetic acid in 100 cc. of the final buffer solution was 0·004 cc.]

The Leishman's stain was prepared by adding 0·16 gm. of Leishman's powder to 100 cc. of the buffer solution. The latter kept the *p*H of the staining solution at approximately 6·4–6·6. The author makes the warning that tap water should not be brought into contact with the apparatus used.

For staining blood smears, the staining solution is added drop by drop until it covers the whole smear, and is then allowed to stand for 4½ minutes. Distilled water is then added in drops until the layer of mixed fluids covers the whole slide. Mixture is effected by gentle tilting. The staining mixture is allowed to stand for 4 minutes and the preparation is then washed with distilled water and dried.

Clear colour differentiation is obtained and the author claims that by using the technique described normochromic may be distinguished microscopically at once from hypochromic bloods, since in the former the red cells appear red or bright pink, while in the latter they stain grey.

Only one malaria smear could be obtained and the parasites stained very satisfactorily. For staining blood smears for parasites the following technique was adopted :—

1. Stain with Leishman stain for half a minute.
2. Add half the amount of distilled water : mix : leave for 10 minutes.
3. Wash in running water for 3 to 5 minutes. Dry.

The author obtained successful results with the solution in airtight flasks after 9 weeks. *H. J. O'D. Burke-Gaffney.*

PESIGAN, T. P. & GARCIA, E. Y. **A Modified Field Stain for Rapid Staining of Thick and Thin Blood Smears.** *J. Philippine Med. Ass.* 1946, Apr., v. 22, No. 4, 165–71. [12 refs.]

When the Philippines were invaded, stocks of staining materials were inadequate, and by April 1942 the authors were almost without Wright and Giemsa stains for blood films. They therefore evolved a substitute as a result of experimental trials with materials then available. They aimed at obtaining a product which would be economical (particularly in methyl alcohol) and which would simplify and shorten the staining process without sacrificing clarity in the preparation.

They eventually chose a method involving three separate solutions, namely :—

I. Methyl alcohol.—Absolute or 95 per cent. for fixation. (Old thin smears and thick blood films do not need fixation, so methyl alcohol can be dispensed with ; but this cannot be done with fresh thin smears.)

II. Basic stain

Brilliant cresyl blue	0·35 gm.
Azure II	0·50 gm.
Borax solution 2·5 per cent.	100·00 cc.

III. Acid counter-stain

Eosine-Y (Water soluble)	0·20 gm.
Distilled water	100·00 cc.

Very full details of preparation and staining technique are given. The principles and history of stains for blood examination are also discussed at length.

The stain described is a modification of a number of familiar ones, notably those of Manson, of MacNeal and of Field.

The authors claim that young red blood cells are recognizable with this stain and they have found it useful for splenic, marrow and brain smears also. Precipitates rarely appear, and the stain is economical, as the solutions may be used several times if kept in Coplin jars. *H. J. O'D. Burke-Gaffney.*

MATHER, K. **The Genetical Requirements of Bio-Assays with Higher Organisms.** *Analyst.* 1946, Sept., v. 71, No. 846, 407–11.

Living organisms such as laboratory animals and plants which are used to measure chemical substances and to test their action, should differ individually as little as possible so that the results of experiments may be as nearly uniform as possible. Variations among individuals of a species may be produced both by environment, which affects chiefly the outward characters (phenotype) and by inheritance by which the actual genetic constitution (genotype) is changed. The environment (*e.g.* feeding, housing) can be standardized to a considerable extent, but to increase similarity by inbreeding a knowledge of genetics is required.

There could be little doubt, and it has in fact been shown, that heritable variation exists between individuals in their reactions to substances for which

they are used as test organisms. Variations due to differences between one or a few genes with large effects (as for example Mendel's tall and short peas) are important in bio-assay; a variant of a fungus due to mutation of such a gene was unable to synthesize a substance necessary to its full development and the variant could therefore be used to assay that substance in the medium in which it was grown [see PONTECORVO, below]. Such mutations have been produced by radiation and were heritable like natural mutations; more commonly, however, a heritable variation is due to the simultaneous action of a number of genes producing similar effects—quantitative or "polygenic" variation.

Asexual reproduction including parthenogenesis, and clonal division (*e.g.* identical twins) produce genetically similar individuals though the occurrence of mutation would cause heterogeneity. Genetical uniformity is also aimed at by inbreeding—self-mating in hermaphrodites and brother-sister or parent-offspring mating in dioecious organisms. Various lines of homozygotes are developed, each line being homogeneous but different from the other lines.

The author refers to various difficulties associated with inbreeding: selection of heterozygotes either by the breeder or naturally through their greater vigour and fertility, and the effect of "inbreeding depression of vigour" on suitability for assay work; the latter can be overcome by using the first cross between two lines, as the heterogeneous offspring are as uniform genetically as their parents, and are more vigorous (see PHILIP *et al.*, *Nature*, 1944, Aug. 26, 260).

There is need for more knowledge of the inheritance of variation in the responses upon which assays are based, of behaviour under inbreeding, and of the comparison between F_1's and their inbred parents; the geneticist and the assayist should exchange information for their mutual benefit. The use of animals with easily recordable characters, *e.g.* piebald coat rather than white, might help to speed up the attainment of homozygosity for that character and at the same time for other characters linked to it and needed for assay. [This paper may remind the research worker on tropical diseases abroad of the need for as much uniformity as possible in the living organisms and in experiments, and in their environment.] [The reader may also wish to refer to CORSON's paper in this *Bulletin*, 1946, v. 43, 169.—Ed.] *J. F. Corson.*

PONTECORVO, G. **The Genetical Aspects of Bio-Assays with Micro-Organisms.** *Analyst.* 1946, Sept., v. 71, No. 846, 411–13.

Although bacteria and most moulds multiply asexually they are not inappropriate subjects for genetic study as they undergo heritable mutation of genes. In microbiological assay the growth response of the microorganism, whether stimulation or inhibition, should have maximum specificity (ideally response to one substance only) and minimum variability.

A pure line of a mould or a yeast can be grown from an ascospore, which has only a single set of genes; the cells, however, are subject to mutation and the consequent heterogeneity is not overcome by repeated single-sporing.

Genetic investigation of bacteria is new but promises to yield valuable results; among recent work is that of DEMEREC (*Ann. Mo. Bot. Gard.*, 1945, v. 32, 131) who found that resistant individuals arose repeatedly in a sensitive strain of *Staphylococcus aureus* exposed to penicillin; resistance was not caused by penicillin but resulted from selection [but see abstract of DEMEREC's similar paper, *Bulletin of Hygiene*, 1945, v. 20, 574]. No means of restricting the development of such resistant forms is at present known.

Most genes act by controlling specific steps in metabolic processes, *e.g.* in the synthesis of arginine by the mould *Neurospora* two genes control the step

from ornithine to citrulline and one gene the step from citrulline to arginine; many other examples are known. A gene can be inactivated by irradiation and the corresponding step blocked; the mutation is heritable, so a strain can be produced which is unable to perform the metabolic process and can therefore be used for an assay of the nutritional requirement for growth in the culture medium (BEADLE, *Chem. Rev.*, 1945, v. 37, 15).

Mutant strains of other fungi and bacteria affecting many processes, such as syntheses of amino-acids and water-soluble vitamins, have been obtained. Artificially produced mutants have advantages over those occuring naturally: requirements can be induced for new substances which no known natural strain requires; the same organism can be used to produce several mutants, each requiring a different nutrilite; and blocks can be produced at the most suitable positions. Once a "perfect" strain is produced it can be used indefinitely, as reverse mutation is unlikely to occur. The genetic technique is simple and collaboration between geneticist and assayist would benefit both.

J. F. Corson.

MONROE, L. & HOPPER, J., Jr. **A Simple Method of determining the Specific Gravity of Small Samples of Urine.** *J. Lab. & Clin. Med.* 1946, Aug., v. 31, No. 8, 934–5.

The method described by the author is a combination of two existing techniques, those of Barbour and Hamilton and of Phillips and associates. Drops of urine are observed in insoluble media of known specific gravities, and there is no need for a watch or for adjusting the mixtures during the test. The method can be applied to measuring the specific gravity of any watery solution.

A series of specific gravities covering the range desired are prepared in 100 cc. lots by mixing xylene and bromobenzene (XBB) [Eastman Kodak, Xylene T275, Bromobenzene No. 43] in the proper proportions [see table].

The urine to be tested is introduced under the surface of successive solutions in the graduated series by means of a dropper. The specific gravity of the urine lies between that of the mixture in which the drop rises, and that in which it falls. If the drop neither rises nor falls in the bottle, the specific gravities of the urine and the mixture are the same.

The xylene-bromobenzene solutions may be made volumetrically (for which a table is given in the text, and reproduced below) or roughly by trial with a urinometer.

Specific Gravity	Xylene (cc.)	Bromobenzene (cc.)
1·005	78·18	21·82
1·010	77·38	22·62
1·015	76·58	23·42
1·020	75·78	24·22
1·025	74·98	25·02
1·029	74·34	25·66

Thus, a 0·16 cc. increase in the quantity of bromobenzene and an equal decrease in the amount of xylene will increase the specific gravity ·001.

For clinical purposes, mixtures in the range 1·005 to 1·029 are usually sufficient. For more accurate work, corrections for evaporation and temperature are described.

If the mixtures become cloudy on repeated use, they may be cleared by filtration through an average-grade filter paper.

The authors point out a number of specialized applications of this method, apart from its value in dispensing with the need for a urinometer. It is a sensitive complementary test to the relatively crude phenolsulphonphthalein test in comparing the kidneys separately, when only a few drops of urine are available after ureteral catheterization: it is useful in the examination of infants, where urine specimens may be scanty, and it is applicable to studies of renal function in small animals. *H. J. O'D. Burke-Gaffney.*

REPORTS, SURVEYS AND MISCELLANEOUS PAPERS.

ROCKEFELLER FOUNDATION. INTERNATIONAL HEALTH DIVISION. **Annual Report, 1945.** pp. ix+147, 14 figs. on 7 pls. New York: 49 West 49th Street.

The work of the International Health Division of the Rockefeller Foundation, with its staff of some 80 trained investigators dealing with health problems in collaboration with Governments and public institutions throughout the world, is too well known and well appreciated to require either introduction or description.

The Annual Report for 1945 once more presents a striking record of vast undertakings launched under the continued vicissitudes of war, for since 1940 the European field had been closed to the Division. During the year the Latin American programme therefore increased proportionately, and indeed its designation for 1945 exceeded those of all other regions combined.

Nevertheless the work adapted to war conditions was continued into the coming of peace, and the Division was ready and equipped to meet the transformation. Researches into typhus fever in the Mediterranean and European theatres were continued in collaboration with U.S. Typhus Commission in the Cairo Laboratories: after the end of hostilities in Europe, a team from the Oxford Nutrition Survey visited the Netherlands and Germany where they studied the pressing problems of deficiency diseases: assistance was also given to the All-India Institute of Hygiene in conducting Dietary Surveys.

The general investigational work of the Division was centred as in previous years, on some 12 diseases, with the major emphasis on yellow fever, malaria and influenza.

Between 1942 and 1945 (in which years the Division's Vaccine Laboratory ceased to manufacture its serum-free yellow fever vaccine) nearly 24 million doses were released. The Rockefeller Foundation Health Commission advised and assisted financially in the establishment of the yellow fever vaccine laboratory in the South African Institute for Medical Research in Johannesburg, where the vaccine for use in Africa is now manufactured. Much useful research on yellow fever was done and has been noted in this *Bulletin*: one particularly important piece of work was the study of the epidemiology of yellow fever in Bwamba County in Uganda. Research was also conducted in Nigeria and in South America.

Work on malaria was carried out in many centres, and dealt, amongst other subjects, with chemotherapy, the exoerythrocytic phase of the parasites, the life-cycle of *P. gallinaceum* and *P. lophurae*, and a great deal of field work concerned to a large extent with the use of the newer insecticides.

The widespread infections with influenza B virus in the U.S. stimulated further work on this and on A virus, principally in connexion with immunology and the production and use of a suitable vaccine.

Endemic typhus and scrub typhus were studied in many fields, and research was made into the value of pediculicides and antagonistic substances.

Many other investigations on infective diseases were undertaken.

Widespread nutrition studies were carried out.

The statement of services rendered to Governments and local Health Services is, as usual, imposing, and includes general and special public health measures, establishment of facilities for health education, schools of nursing and other training. Fellowships in seven subjects were granted to 115 persons. The Report ends with a complete list of expenditure on Public Health work from 1913 to 1945.

This report demonstrates once more, if demonstration were needed, the high aims and the admirable results which the Rockefeller Foundation, through this unit of its five divisions, continues to extend to human welfare and the relief of suffering. *H. J. O'D. Burke-Gaffney.*

TROPICAL MEDICINE NEWS. Bethesda, Md. 1946, June, v. 3, No. 3, 14.

Incidence of Insect-borne Diseases in U.S. Army during World War II.

The following provisional figures of insect-borne diseases in the U.S. Army during the recent war are given by Lt.-Col. McCoy, Chief of the Tropical Diseases Control Branch, Surgeon-General's Office, U.S. Army :—

Disease	Cases	Rate per 1,000 per year
Malaria	440,789	20·0
Dengue	82,392	3·7
Sandfly fever	12,228	0·5
Typhus fever (total)	7,269	0·3
Scrub typhus	6,803 (estimated)	—
Endemic typhus in U.S.	402	—
Epidemic typhus	61 (estimated)	—
Filariasis (Wuchereria)	2,110	0·09
Leishmaniasis	344	0·02
Relapsing fever	241	0·01
Rocky Mountain spotted fever ...	60	0·003

It is noteworthy that no onchocerciasis, plague, yellow fever, oroya fever or trypanosomiasis was recorded (although two cases of *T. cruzi* infection are known to have occurred in soldiers in Panama).

The malaria figures include readmissions to hospital, but do not include statistics from the Philippine Islands prior to October 1944, as records were lacking.

The filariasis infections (*W. bancrofti*) were acquired almost entirely on certain S. Pacific islands in the early days of the war.

The figure given for leishmaniasis includes both visceral and cutaneous types : it is not, however, complete as many of the cutaneous cases were seen as out-patients without being absent from duty. It is estimated that some 800 cutaneous and 60 visceral lesions occurred amongst members of the Army.

H. J. O'D. Burke-Gaffney.

BIGGAM, A. **Wartime Advances in Medicine which might be translated into Civil Practice.** *Edinburgh Med. J.* 1946, Aug., v. 53, No. 8, 413–28.

This article is a brief summary of the important advances made in the field of [tropical] medicine during the war years: further condensation can only be achieved by enumeration.

Against insect transmitters of disease, the now world-famous insecticide, DDT (dichlor-diphenyl-trichlorethane) came into general use and the more potent benzene hexachloride (666) was discovered. The general insect repellent, dimethyl-phthalate (DMT), and the miticides, dibutyl-phthalate (DBT) and benzyl benzoate—the latter being particularly useful in scabies—were introduced.

For malaria control, in addition to DDT—which was used extensively against both the adults and larvae of anophelines—and the repellents mentioned above, mepacrine (atebrin) was put on a sound basis as a suppressive as well as a curative drug: a daily dose of 0·1 gramme will suppress benign tertian malaria as long as it is being taken and if maintained for one month after the subject leaves an endemic area, it will "cure" subtertian malaria. For the complete cure of benign tertian malaria, pamaquin (plasmoquine) 0·03 gramme *plus* quinine grains xxx daily for ten days has been shown to be the most effective combination. [This last observation must surely be classed as one of the war's rediscoveries—*vide* this *Bulletin*, 1929, v. 26, 14.]

Paludrine, which did not appear until the end of the war and did not come into general use is, apparently, a true causal prophylactic as far as malignant tertian malaria is concerned, and in doses of 100 mgm. daily acts as a more efficient suppressive of benign tertian than does mepacrine.

New drugs have altered the whole outlook in bacillary dysentery. The British favoured the relatively insoluble sulphaguanidine (5 gm. every three hours for the first 24 hours), the Americans the more soluble sulphadiazine. More recently two other drugs have been introduced and may replace each of the former when they have had a longer trial: these are phthalyl-sulphathiazole and sulphamezathine, the latter having the advantages of high solubility without the disadvantages of liability to cause kidney damage. The practice of administering these drugs immediately on the first appearance of diarrhoea cut down the incidence of bacillary dysentery in the Army to a remarkable degree. Bacteriophage therapy was decently buried.

No quick cure for amoebic dysentery was found. A notable advance was made by the use of penicillin and the sulphonamides in conjunction with the amoebicidal drugs in the treatment of the chronic condition; doses of 30,000 units every three hours up to two million units of penicillin, and of 10 to 20 grammes daily of one of the sulphonamides, are given. The routine course for chronic amoebiasis includes penicillin and phthalyl-sulphathiazole for 8 days, chiniofonum (yatren) enemata for 12 days (or diodoquin by mouth for 20 days), and carbarsone or stovarsol for 12 days, followed by a period of observation for 4 months with repeated stool-examinations.

The low incidence of epidemic typhus can be attributed to DDT and vaccination. A reduction in the incidence of scrub typhus was brought about by the extensive use of the miticide, dibutyl-phthalate; the vaccine for this infection arrived too late for a satisfactory field trial.

The sulphonamides, whose value in cerebrospinal fever is well recognized, proved useful for the elimination of carriers. Doses of 3 grammes a day for three days of sulphadiazine or sulphathiazole were adequate.

Penicillin is of doubtful value in Weil's disease, but successful in both forms of rat-bite fever. In the rapid form of treatment of syphilis, 2–4 million units

of penicillin given in 7½ days will cure primary Wassermann-negative cases, but the relapse rate with primary Wassermann-positive cases is too high for safety.

For sea-sickness, 1/100 gr. hyoscine one hour before embarking, repeated in 6 hours' time, was found the most successful.

Among advances in laboratory diagnostic methods, the demonstration of elementary bodies in smallpox vesicles, and the rickettsia differential agglutination in typhus fevers, are mentioned.

Other subjects discussed include psychiatry, physical development centres, military convalescent depots, and administration, in all of which the author considers that from Army experience we have learned much that can be applied in civil life. *L. E. Napier.*

WHITE, J. G. **Administrative and Clinical Problems in Australian and British Prisoner-of-War Camps in Singapore, 1942 to 1945.** *Med. J. Australia.* 1946, Sept. 21, v. 2, No. 12, 401–3.

EDDEY, H. H. **Prisoner-of-War Camps in Borneo.** *Med. J. Australia.* 1946, Sept. 21' v. 2, No. 12, 403–4.

O'BRIEN, H. R. **Health Conditions in certain Large Cities of the Far East after Liberation.** *Pub. Health Rep.* Wash. 1946, Sept. 13, v. 61, No. 37, 1339–50, 4 figs.

The author was Chief Medical Officer of the Philippine Mission and of UNNRA in the Far East and made observations on the prevalent diseases of seven of the chief cities, one each of Burma, Siam, Indo-China, the Philippines, Malaya, the Dutch East Indies, and Hong Kong. A few remarks are made on each of these. In all were to be seen the results of bomb-damage, interference with water-supply, housing difficulties and food shortage. In Rangoon, smallpox accounted for some 8 cases weekly [probably there were others which were not notified] from May 1945, with a 50 per cent. fatality. Plague, cholera, chickenpox and mumps were present, but only a few cases of each. Bangkok had a serious smallpox epidemic with a high fatality of 50 per cent., and cholera was rife (144 deaths in May 1945). In Saigon, malaria, dysentery and beriberi were serious. The Pasteur Institute continued to prepare vaccines against smallpox, cholera, plague, rabies, typhoid, dysentery and influenza. In Manila, deaths from starvation were many and the chief diseases causing death were pulmonary tuberculosis, beriberi, dysentery and pneumonia. In Singapore, the main mortal diseases were, as was expected, malaria, dysentery, tuberculosis and beriberi. The last, between September 2nd and October 6th, 1945, caused 16·2 per cent. of all deaths. To avert epidemics, some 100,000 persons were vaccinated against smallpox and enteric fever, from September to December inclusive. A small poliomyelitis outbreak developed in February 1946 [nothing is said as regards the number of cases except " Following 22 cases in the British military services, starting in late November, civilian cases began to appear . . ."]. From 1935–38 diphtheria mortality ranged from 9·8 to 12·0 per 100,000, but owing, it is thought, to the immunization efforts of the Japanese, there were no deaths from this cause till January 1946. In Batavia, overcrowding and bad hygiene resulted in, or were followed by, typhoid, dysentery and a measles outbreak. In Hong Kong the usual overcrowding was intensified by the influx of 750,000 refugees, increasing the normal population by 75 per cent. Malaria was rife and tuberculosis was one of the chief causes of death, accounting for 10·4 per cent. of all deaths in the six weeks, February 14th–March 23rd, 1946. Typhoid, diphtheria, cerebrospinal fever and cholera were also present, but only in small numbers. *H. Harold Scott.*

DERHAM, A. P. **Singapore and After : a Brief Historical Survey of the Activities of the Australian Army Medical Corps in Malaya.** *Med. J. Australia.* 1946, Sept. 21, v. 2, No. 12, 397–401, 1 map.

JANNONE, G., FERRO-LUZZI, G. & MARA, L. Risultati di una spedizione tecnico—Scientifica nella Dancalia Settentrionale Esterna. (Studio agrario, entomologico, malariologico e di fisiologia alimentare. [**Results of a Technico-Scientific Expedition in the Outer Northern Danakhil Country : Agricultural, Entomological, Malariological and Nutritional Studies.**] *Boll. Soc. Ital. di Med. e Igiene Trop.* (Sez. Eritrea.) 1946, Monograph No. 2, 167 pp., 23 figs. & 2 folding maps. [63 refs.] English summaries.

The authors, accompanied by Major K. J. Grant, R.A.M.C., made a tour lasting a month through the Danakhil Desert, and their report gives the results of their explorations. Very little has hitherto been published about this tract of country, a fact that endows this report with added interest.

The Danakhil country lies along the western shore of the Red Sea from 12°22′ to 15°30′ N. latitude. It comprises some 25,000 square kilometres, inhabited by rather less than 20,000 people. It is a barren, inhospitable country, partly mountainous, partly flat, and completely isolated from European civilization. Unfavourable climatic conditions, sterility of the soil, lack of roads, scarcity of water, no agricultural possibilities, and lack of trade with the outside world account for the isolation of its people. The activity of the people is mainly pastoral—goats, sheep, a few herds of cattle and some camels, donkeys and mules. Except for dwellers on the coast the pastoral community is nomadic, a nomadism compelled by the need of food and so controlled by the rainy seasons. Members of one tribe rarely if ever enter other tribal areas.

Climatic and ecological conditions generally are unfavourable to mosquitoes. Malaria is restricted to two small areas, the remainder of the country being almost entirely free from the disease. In the extreme north, conditions resemble those in other parts of Eritrea where *A. gambiae* is responsible for the spread of malaria. The second malarious locality is in and around Assab, where the vector is *A. culicifacies* var. *adenensis*. Other anophelines that were found in the Danakhil country were *A. d'thali*, *A. dancalicus*, *A. rupiculus*, *A. funestus*, *A. rivulorum* and *A. turkhudi* ; none of them is of local importance as a malaria vector.

Four species of *Aëdes* were identified, *aegypti*, *caballus*, *arabiensis* and an unusually pale form of *vittatus*. *Aëdes aegypti* was confined to coastal towns.

Shepherds in the mountainous areas subsist on a diet composed exclusively of raw goats' milk. No gross evidence of malnutrition was seen among people on this milk diet. In the lowlands the milk diet is supplemented with a small amount of meat and " dura " (*Andropogon sorghum*) when milk is scarce. In the coastal areas, where social conditions are extremely poor and there is no pasturage, the diet is mixed but deficient. It consists of variable amounts of milk, meat, fish, cereals and the fruit of the " Dum " palm. Gross evidence of malnutrition is more common on the coast than elsewhere.

Norman White.

BOOK REVIEWS.

INDIA. **Report of the Health Survey and Development Committee** [BHORE, J., K.C.S.I., K.C.I.E., C.B.E., Chairman]. **Vol. I. Survey.** pp. vi+228. **Vol. II. Recommendations.** pp. 2+vi+532. **Vol. III. Appendices.** pp. iv +351. **Vol. IV. Summary.** pp. vi+90. 1946. Delhi: Manager of Publications.

This important report contains the findings of a Committee appointed by the Government of India in October 1943 to survey health conditions and health organization in British India, and to make recommendations for future development.

The Chairman of the Committee was Sir Joseph Bhore, a very able and distinguished retired officer of the Indian Civil Service, who had quite exceptional qualifications for presiding over the enquiry. The other 24 members of the Committee were chosen with the object of forming a team fully representative of enlightened Indian and European opinion. Including the chairman, 19 were Indians; 16 of these were men, 11 of whom were medical, and three were women, of whom two were medical. Five of the six European members were medical men, and all of them, like their Indian colleagues, had intimate knowledge of conditions in India. Among the Indian members there were representatives of all the great religions and of various shades of political opinion.

The state of health of the people of India was estimated on the basis of certain statistics, including the recorded death rate of 22·4 per mille and infant mortality rate of 162 per mille in 1937, and the expectation of life, at birth, of 26·7 years for the period 1921–1930. Another highly significant figure is stated:—nearly 50 per cent. of all the deaths in India were among children under 10 years of age, whereas in England and Wales the corresponding percentage is about 10.

Dr. Aykroyd is quoted as stating that "an insufficient and ill-balanced diet is typical of the food consumed by millions in India." The diet of Indians consists of cereals to the extent of 80 to 90 per cent., and during the period 1939–1943, the production of cereals was estimated as being 22 per cent. short of the needs of the people. Such important foods as milk, vegetables, fruits, meat, fish and eggs are said to be available in quantities which need to be increased several-fold to provide a well-balanced diet.

The inadequacy of the medical and health organizations is fully described; there is one doctor to 6,300 persons, one nurse to 43,000, one midwife to 60,000, and one qualified pharmacist to 4,000,000. In rural areas the situation is very much worse; in the United Provinces there is one doctor to 105,000; the most favourable ratios are in Sind and the Punjab which have one doctor to 22,904, and one to 30,925 of the rural population, respectively.

The adverse influence of certain social customs is discussed; the observance of *purdah* is said to be responsible for an appalling degree of prevalence of tuberculosis among young women. and the maternal mortality rate is much higher among child mothers under the age of 15 than among those of the higher age groups; it is 46·51 per 1,000 confinements under 15 and progressively declines to 17·91 for mothers of the 20–24 age group.

The history of the development of health administration in India is recounted, and a description is given of the present organization of medical relief and public health.

An interesting chapter deals with the nutritional problem; it is stated that the total wages of many workers would not be enough to provide a satisfactory diet for their families.

In the chapter on Vital Statistics it is shown that the registration of births and deaths is grossly defective; when the recorded figures are checked at the

end of each 10-year period by the "reverse survival" method the following discrepancies have been found :—

	Birth Rate		Death Rate	
	Recorded	Estimated	Recorded	Estimated
1891–1901	33	46	31	44
1901–1911	37	49	33	43
1911–1921	37	48	34	47
1921–1931	33	46	25	36
1931–1941	34	45	23	31

In the detailed survey of the whole field of health effort a frank statement is made of the serious defects, quantitative and qualitative, of the various organizations ; the only one of the 14 chapters dealing with this subject that can be read with any feeling of satisfaction is the last, entitled "Medical Research", in which a well-deserved tribute is paid to a large number of institutes and organizations which have made important contributions to knowledge.

In their Recommendations the Committee propose that development should be progressive ; full details are given of a Short-Term Plan covering two periods of five years each and of a Long-Term Plan which ought to come into force by the end of ten years. For both plans it is proposed that units of population of about three millions each should be dealt with in preference to the present districts, whose population varies from a few hundred thousand to more than five millions. Each unit would have a District Health Centre which eventually would have hospitals with a total number of 2,500 beds, and which would be the headquarters of the whole district health organization. There would be five Secondary Health Centres and 30 Primary Health Centres.

Close co-operation between medical relief and public health is proposed ; the staff would be on a whole-time basis, but when suitable private practitioners are available honorary part-time doctors would be employed.

The increase in medical personnel needed by 1971 would involve approximately a four-fold increase in the number of doctors, a hundred-fold increase in nurses and health visitors, a twenty-fold increase in midwives, an eight-hundred-fold increase in pharmacists, and a ninety-fold increase in dentists.

The Committee recognize that no plan can succeed unless the nutritional condition of the people can be greatly improved ; they state that food planning should aim at "the provision of an optimum diet for all, irrespective of income." Unfortunately the prospect of achieving this standard of nutrition is regarded as depending on the possibility of :—(1) more than doubling the present production of milk or the large-scale manufacture of synthetic milk ; (2) the provision of several times more fish than at present ; and (3) the large-scale production of urea as a food for cattle (urea is converted by cattle into protein).

The capital non-recurring cost of the scheme, spread over ten years is estimated to be, 3,629,900,000 rupees (13½ rupees=£1), and the total recurring cost, spread over ten years, would be 6,018,200,000 rupees. These sums sound colossal for a poor country like India, but the highest yearly cost, reached in the tenth year of the scheme, would be less than three rupees for each person. Some suggestions are given of the ways of raising the necessary funds, but undoubtedly the financial proposals will meet with a good deal of opposition.

The relatively small part of the Report that deals with the Population Problem is highly significant ; it is the first realistic pronouncement on the subject by a representative committee. A few points from the findings are as follows :—

"The need for a constant adjustment between population and the resources available should receive serious consideration."

The population of India has increased during each decade since 1872, but the average rate of increase during the first five of the ten-year periods since that time was only about 4 per cent. Between 1921 and 1931 the rate was 10·6 per cent., and between 1931 and 1941 it was 13·6 per cent. During these 20 years the population of India increased by 83 millions.

The Committee point out that if the proposed health services should succeed in preventing half the present number of deaths, the rate of growth of population would be eight millions a year, so that "a purposeful control of mortality without a corresponding fall in the fertility rate of the community can thus have far-reaching consequences."

It is considered essential that plans for the future, in public health and other matters, should take into account a forecast of the probable population; and regret is expressed that no tabulation was made of the age and sex composition of the population in the 1941 census.

The only important artificial check that has been imposed on growth of population in India is the prohibition of remarriage of Hindu widows; Kingsley Davis estimates that if this ceased to operate there would be a net gain in fertility of 14 per cent.

The situation is summed up in these words:—"it is our considered opinion that the growth of population in India will become an increasingly serious problem."

Various solutions are discussed; relief by emigration is regarded as impracticable; increased production of food and other commodities "will be only a temporary expedient, because a limit to economic production will be reached sooner or later, and uncontrolled growth of population must, as far as we can see, outstrip the productive capacity of the country." Improvement in the standard of living is regarded as tending to cause a fall in the birth rate "by helping to create an incentive in individuals to limit the size of their families", but it is recognized that this improvement must be a slow process and that the proposed health services and other uplift measures "will result in an appreciable reduction of the death rate and thus produce a temporary acceleration of the rate of growth of the population."

The Committee conclude that "we seem to be left with birth control through positive means as the only method that is likely to be effective," and that the only practical steps that can be taken are:—(1) "a relentless pursuit of the measures that are now being proposed—to raise the standards of life," and (2) the spreading of the knowledge of birth control as far as the limits imposed by the present circumstances of the country will permit.

An important recommendation is that an organization for the continuous study of the population problem should be set up by Government.

The significance of the above findings is greatly increased by the fact that the Committee was so fully representative of all sections of the Indian and European communities in India; among the 25 members only one dissented from the views on the population problem; this member, a European medical officer, has expressly dissented—for reasons which are not stated—from the part of the Report dealing with the population problem. One of the several Hindu members "was unable to subscribe to all the recommendations contained in the Report." Apart from these two members all the others have signed the report without reservation. This high degree of unanimity must reassure those who fear that a frank discussion of the population problem is likely to give offence to Indians.

The survey of the health situation in India is admirable, it goes to the root of the matter by showing the need for a bold policy of improvement in the

health organization while at the same time pointing out that a sound public-health policy must be based on a satisfactory state of nutrition, which in turn depends not only on increased production of the necessities of life but also on the restriction of the inordinate growth of population.

The recommendations for development are equally admirable, up to a point, but in view of the clear statement that the success of the Plan depends on the maintenance of a favourable balance between available resources and population, the recommendations for securing this balance come as something of an anti-climax. The Committee could not have been expected to produce a ready-made plan for solving the terribly complicated population problem, but they might at least have sounded a loud note of warning that there is an urgent need for a thorough investigation into the problem, seeing that their own findings have shown that a solution must be found if disaster is to be averted.

The Committee have, in fact, produced excellent plans for a new public-health edifice for India, and have pointed out that this will collapse unless a sound foundation is prepared ; they have also stated the general principles on which this foundation should be constructed, but the impression conveyed by the recommendations is that the erection of the edifice should be undertaken forthwith in the hope that somehow a secure foundation may be provided.

The experiment carried out by the U.S.A. since 1900 in Porto Rico has demonstrated that modern medicine and sanitation, even when backed up by universal education and intensive economic development, have failed to create satisfactory conditions of life in a population whose birth rate has remained almost stationary at about 40 per mille, while the death rate has fallen to about 20 per mille. In the report dated 1940, of a committee appointed by the late President Roosevelt, it is stated that " unless the population problem is solved, all else is ' whistling in the wind.' "

There is no reason to expect that the results of a similar experiment in India or any other over-populated country would be better in the absence of purposive restriction of the natural rate of growth of population. *John W. D. Megaw.*

MACLEOD, J. M. H. [M.A., M.D., F.R.C.P.(Lond.), etc.] & MUENDE, I. [M.R.C.P.(Lond.), M.B., B.S., B.Sc.(Lond.)]. **Practical Handbook of the Pathology of the Skin. An Introduction to the Histology, Pathology, Bacteriology, and Mycology of the Skin with special reference to Technique.** 3rd Edition. pp. xix+415, 27 coloured & 125 black & white illustrations. 1946. London : H. K. Lewis & Co. Ltd. [50*s*.]

This handbook was first published in 1902 by J. M. H. MacLeod ; a second edition was issued in collaboration with I. Muende in 1940 and, despite the limitations set by hostilities on its distribution, this edition was exhausted within four years.

The present volume does not differ greatly from its immediate predecessor and is an excellent and extremely practical work which will be valued at home or abroad by those who are interested in the histo-pathology of the skin. No small part of its merit is that it is essentially a book for the practical pathologist and the practising clinician ; all the important details, so often omitted from more pretentious works, are carefully set down, so that the reader can have little excuse for faulty biopsy technique, or for errors in the all-important tasks of fixing, hardening, embedding, cutting and staining. This last matter—the proper staining of sections of skin—is an art which is not widely studied, and in many laboratories it seems to be believed that a standard haematoxylin and eosin stain is all that is required ; therefore it is encouraging to note that

throughout the book emphasis is placed on the importance of using particular stains for particular purposes, and to find that full instructions are given as to how these special techniques should be employed. Despite the insistence on these laboratory details, the main part of the work is devoted to an explanation of the architecture of the skin, its embryology, and the pathological changes which can occur in the epidermis and corium, and in the hair and nails.

The arrangement of the subject-matter is particularly attractive to the clinician who will appreciate the scheme of classification and the thumb-nail sketches of the clinical features of each malady which are given before the histological changes are discussed. The descriptions both of microscopic and macroscopic abnormalities are accurate, comprehensive and lucid.

Those engaged in the study of tropical medicine may find the references to tropical maladies somewhat brief, but many of the diseases which are relatively common at home, such as tuberculosis of the skin, seborrhoeic eruptions and eczema, are common overseas, and the book will certainly be as useful to the dermatologist abroad as to his colleague in Britain.

The illustrations and the captions attached to them are very satisfactory, and the handbook can be recommended as an invaluable *vade-mecum.*

R. M. B. MacKenna.

ANDREWS, George Clinton [A.B., M.D., Associate Clinical Professor of Dermatology, College of Physicians & Surgeons, Columbia University, etc.]. **Diseases of the Skin. For Practitioners and Students.** 3rd Edition. pp. vi + 937, 971 illustrations. 1946. Philadelphia & London: W. B. Saunders Company. [$10.00.]

This text-book has an international reputation. Its merits are manifold and its scope is sufficiently wide to include most of the skin diseases seen in tropical and subtropical countries as well as in temperate zones. The author has not wasted space and money in coloured pictures, and in making this decision he was probably wise, for colours are still erratic, whereas many of the black and white illustrations which fill his pages are superb, and are an invaluable aid to diagnosis.

The book commences with the usual introductory chapters, and follows the examples of earlier editions by stressing details of roentgen and radium therapy and the use of surgical diathermy in dermatological practice. Thereafter, with the exception of the last chapter, which is contributed by Carl B. BRAESTRUP and is devoted to the physics of roentgen rays, the book is devoted to the study of cutaneous diseases. At the conclusion of each chapter a short list of references is given.

Because of its wide scope, the book is of most value to those interested in problems of diagnosis; in the consideration of most diseases, adequate reference is made to the histo-pathology of the lesions, and often there is a helpful illustration of the microscopical appearance of a biopsy specimen. Those working with the resources of a fully equipped department will value the discussions of the various electro-therapeutic measures which may be employed and the suggestions concerning radium therapy, but those working "out in the blue" will not find the sections in therapy as helpful as their more fortunately-placed colleagues who have but to press a couple of switches to have their therapeutic powers enhanced by the force of some sixty thousand volts. Further, in many instances the author is content to give a list of applications which may be employed, without giving specific instructions concerning the indications for their use; this device is helpful to the specialist or to one who

has considerable experience in dermatology, but is less helpful to those who have limited experience in this branch of medicine. It is, in fact, the sections on therapy which are most vulnerable to criticism ; thus, the use of oestrogens in the treatment of acne vulgaris, sulphapyridine in chronic lupus erythematosus, and formalin bathing for plantar warts, do not receive mention in the appropriate paragraphs. Sulphapyridine is extolled for the treatment of dermatitis herpetiformis, but no warning is given concerning the paramount necessity of controlling its administration carefully by frequent survey of the blood picture.

These, however, are but minor defects in a book which is a monument of endeavour and has few rivals in its own particular place among dermatological text-books. *R. M. B. MacKenna.*

COCKER, Dorothy E. [S.R.N., S.C.M., etc.]. **Aids to Tropical Nursing.** With Foreword by L. E. NAPIER, C.I.E., F.R.C.P., Director, School of Tropical Medicine, Calcutta]. Second Edition. pp. xi+218, 17 figs. 1946. London : Baillière, Tindall & Cox, 7 & 8, Henrietta Street, Covent Garden, W.C.2. [5*s*.]

The demand for a second edition of this text-book in such a short time shows not only that there is a great need for a reliable text-book on tropical nursing, but also that this volume goes far to meet this need. The first edition was itself a very useful book : as a result of experience gained and of criticisms written about the first edition, however, several additions have now been made. The chapter on nutritional disorders has been enlarged, a new chapter on the care of children in the tropics has been included and several additional ailments have been dealt with. These add considerably to the value of the book from the point of view of the nurse, but even more from that of women generally in the tropics. The increased attention to the preventive aspect is also a decidedly helpful addition and the grouping of the diseases according to their mode of transmission instead of in alphabetical order is a more rational method.

The book forms one of a series of text-books dealing with the various branches of nursing written, in most cases, by sister tutors in prominent hospitals. Each book is intended to be a complete text-book in itself, the title " Aids to Tropical Nursing " indicating that the books are aids to knowledge and not just aids to the study of larger books. On the whole this claim can be considered fairly well-justified in the case of the present volume, but a few suggestions for future editions might be made. Thus, in places the book appears to be written with conditions in India in mind rather than with those throughout the tropics ; a wider outlook would make the book more useful. Again, one of the greatest needs of nurses in the tropics to-day is for information on the special arrangements, and the adaptations, which are so frequently required in hospitals there, expecially in smaller rural hospitals. Information is required, for example, on the special care required in the storage and care of hospital equipment, on the utilization of local materials, on the adaptations often required in hospital administration and routine to suit the local conditions and customs of the people.

A considerable amount of knowledge by nursing sisters on these matters has now been gained in many parts of the tropics. A chapter giving information on these most important matters would be very helpful, especially to newcomers.

Dr. Napier in his foreword to this book draws attention not only to the great shortage of well-trained nurses in the tropics, but also to the disproportionate shortage of nurses compared with the number of doctors—though the number of doctors is still very inadequate. While this volume cannot of itself increase the number of student nurses, it should go a long way to improving the education

of those students who do present themselves for training, and should be of great help to nurses in Britain who are preparing to undertake nursing duties overseas. *Mary G. Blacklock.*

NICHOLLS, Lucius [C.M.G., M.D., B.C., B.A.(Cantab.), etc.] [Edited by]. **Aids to Tropical Hygiene.** 3rd Edition. pp. xii+217, 6 pls. 1946. London: Ballière Tindall & Cox, 7 & 8, Henrietta Street, Covent Garden, W.C.2. [6s.]

"The general principles for the practice of Public Health are the same throughout the world." On this admirable text, Dr. Nicholls opens his Preface to the 3rd edition of a work which, by extension of this too frequently ignored premise, might itself, with advantage have been entitled "Aids to Hygiene in the Tropics."

It is inseparably in the nature of a work of this kind, which serves to guide its reader to the larger text-books rather than to dispense with them, that it should be highly condensed and concentrated: hence some degree of generalization and apparent dogmatism becomes almost inevitable. In common with so many "refresher" books, this work is not altogether free from statements with which not all authorities will necessarily agree, particularly in relation to more controversial matter: but this is perhaps a defect in the scope rather than in the preparation of such a book; and it is more than offset by the immense amount of factual matter which Dr. Nicholls and his collaborators have succeeded so admirably in compressing between little more than 200 small pages.

The book is divided into 3 parts, namely: Parasitology; Food and Nutrition; and General Public Health work, written respectively by Drs. V. SIVALINGHAM, D. B. GUNASEKARA and O. E. R. ABHAYARATNE, under the general editorship of Dr. Nicholls.

In his Preface, the editor discusses the effects of warm climates on health, and the scope and purpose of hygiene in the Tropics.

The first section deals with all the common ecto- and endoparasites and the diseases produced by them, and is illustrated by simple but very clear drawings.

The second section discusses food constituents and requirements, and gives useful information on prescribing diets, on malnutrition and on food poisoning.

The last section covers the general range of public health work, with special relation to tropical conditions and requirements, and including such special features as the sanitation of festivals and pilgrimages and port hygiene and quarantine. Practical information is given on disinfection and the preparation of vital statistics, and on the control of communicable diseases [a number of the specific names require bringing up to date]: reference is made to the newer insecticides and to methods of malaria control. This section ends with a brief and somewhat sketchy chapter on Maternity and Child Welfare, which tends to lean rather too heavily, in the reviewer's opinion, on generalizations, which in the condensed compass of so vast a subject, are least likely to be factually informative to a reader not already familiar with this speciality.

Throughout, the authors have adopted the admirable practice of tabulating material, wherever possible, and useful tables are found in every section describing, for example, the differences between species of parasites, the characters of various diseases, food constituents, diets, differential diagnoses, analytical data, and the like.

The carefully prepared and clearly produced line-illustrations by Mr. T. D. DE ALWIS add considerably to the value of this Edition, which now takes its place amongst the "Aids" series as a useful outline of the general principles of hygiene in warm climates. *H. J. O'D. Burke-Gaffney.*

TOBBACK, L. [Docteur en Médecine Vétérinaire, attaché au Ministère des Colonies]. **L'inspection des viandes au Congo Belge.** [Meat Inspection in the Belgian Congo.] 85 pp., 9 figs. 1946. Brussels: Imprimerie A. Beirnaerdt, 41, Rue des Coteaux. [15 Fr.]

An Ordinance published in the Belgian Congo in 1935 prescribed that where possible all inspection of fresh meat should be undertaken by veterinary officers, and failing that, by medical officers or others adequately qualified: but where such qualified persons were not available, District Commissioners could, in exceptional cases, appoint as meat inspectors anybody whom they were satisfied were fitted to undertake that function.

The purpose of this handbook is to provide in readable form all the information necessary to enable a meat inspector to undertake this work.

The book opens with a discussion on the purposes and scope of meat inspection, and passes to a description of the slaughter of domestic animals, the technique of inspection, the points to be observed in examining an animal, and various useful anatomical and physiological descriptions, illustrated in part with diagrams.

The various defects and diseases likely to be encountered are then described at length, together with the significance, from the point of view of edibility, of different pathological states.

There follow sections which will be of special interest to the worker in the Tropics, for they include descriptions of parasitic and mycotic diseases of domestic animals, with a special reference to tropical diseases. A short note on the sterilization of meat is included.

There are four useful Appendices to the book, consisting respectively of a list of anatomical points to be noted in meat inspection; a table showing anatomical differences in sex and species between the commoner slaughter-animals and the changes in meat derived from them; extracts from the Belgian laws relating to meat for human consumption; and the procedure in force in Belgium for dealing with tuberculosis in animals used for food.

The reviewer is not aware of a handbook in English especially designed for meat inspectors in the Tropics, and this well planned and set-up volume should prove of very great value to those concerned who read French.

H. J. O'D. Burke-Gaffney.

LIVADAS, Gregory A. [M.D., M.P.H., Director of Athens School of Hygiene, etc.] & SPHANGOS, John C. [M.P.H., etc.]. **Malaria in Greece (1930–1940). Research—Control.** 1941. Vol. 1. pp. viii+238, 86 figs. & numerous illustrations, maps & diagrams and 1940. Vol. II. pp. vi+299, 246 figs. & 18 maps. Athens: "Pyrsos" Press Ltd.

This book was published in Athens in 1941, both in Greek and in English, but copies have only recently been received in England. The introductory chapters give a succinct account of the geography, climate, administrative organization and public health administration of the Kingdom of Greece. The somewhat chequered history of public health activity is outlined. The establishment of the Athens Health Centre and School of Hygiene in 1929, with the collaboration of the Health Organization of the League of Nations and of the International Health Division of the Rockefeller Foundation, marked the beginning of a period of intensified public health activity. The Malaria Division of the School of Hygiene started under the technical direction of a member of the staff of the Rockefeller Foundation and the Foundation continued to collaborate throughout the period covered by this report.

In these two volumes are gathered together comprehensive accounts of the results of malariological research, malarial surveys and malaria control

measures carried out in many parts of Greece during 1930 to 1940. It is a proud record. Much of the work will be familiar to students of malaria literature from reports published by BALFOUR, BARBER, RICE, SHANNON and Greek malariologists, prominent among whom are the authors of these volumes, the senior being the Director of the Division of Malariology and Tropical Diseases of the Athens School of Hygiene.

The biology and geographical distribution of Greek anophelines are well described: *A. maculipennis*, *A. superpictus*, *A. elutus*, *A. bifurcatus*, and *A. algeriensis*. *A. hyrcanus*, *A. plumbeus* and *A. marteri* also occur but are not so widely distributed.

The procedure and technique adopted in carrying out very numerous antimalarial programmes are fully described, and very numerous photographs, charts and maps add much to the interest of the narrative. Little or no use had been made of spray-killing adult mosquitoes, as an antimalaria measure, up to 1940.

The work recorded in these volumes is a credit to all concerned.

Norman White.

AIR MINISTRY. **Principles of Anatomy and Physiology for Physical Training Instructors in the Royal Air Force.** A.P. 3125. pp. vi+180, 158 figs. 1946. London: H.M. Stationery Office. [7*s*. 6*d*.]

This manual is intended to provide physical training instructors in the Royal Air Force with a sufficient knowledge of anatomy and physiology to enable them to have a better understanding of their work.

In view, however, of its simple and readable form, it is suggested that it might be of equal value to those engaged in teaching Africans and others who undergo modified medical courses in which a short course in these subjects is required.

One or two short chapters, *e.g.*, "Fitness for Flying" and "The Instructor's Part in Rehabilitation" are of course too specialized for the purposes indicated above: but the greater part of the book is taken up with information which will be found valuable. The illustrations are admirably simple, clear and well presented.

H. J. O'D. Burke-Gaffney.

GREAT BRITAIN: SCIENTIFIC INSTRUMENT MANUFACTURERS' ASSOCIATION OF GREAT BRITAIN, LTD. **Handbook with Classified Index of Instruments.** pp. 48 + 73. [Private and Confidential, not to be published.] 1946. London: 123, Pall Mall, S.W.1.

This handbook should prove useful to Medical Storekeepers and others concerned in purchasing scientific instruments.

It contains an alphabetical list of products and the manufacturers' Code Numbers, together with a handy thumb index referring to the full addresses of the various firms concerned.

Each page of the index is devoted to details of a particular firm and its products.

H. J. O'D. Burke-Gaffney.

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